Chapter 3

Social issues

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1 Introduction

Gene drive organisms (GDOs) are a new biotechnological development that currently has no final product available to be assessed for its risks and benefits to society. In the first part of this chapter, we look at where investment in gene drive R&D is coming from, along with how conflicts of interest may arise. We examine the promises made about what products we can expect from this technology, especially in terms of claims about how they would benefit society and the economy. We also discuss how such promises influence public understanding of the technology and help to secure research funding. We then examine gene drive patent applications. In the second part of this chapter, we examine how issues such as consent and risk assessment have been tackled by existing projects using genetically modified (GM) mosquitoes (currently without gene drive, but with some plans to include it in the future) and discuss liability and the Precautionary Principle. Finally, we discuss what more meaningful public engagement about these issues would require.

2 Gene Drive science in context: science in society

Research and development of gene drive organisms (GDOs) is taking place in different social and economic contexts across the globe. For gene drive organisms (GDOs), the initial investment in R&D occurs mainly in rich economies (notably in the USA, Australia, the UK and some other European countries). In contrast, some of the first open releases of GDOs are planned in resource-poor countries, with the claim that they will tackle diseases of poverty such as malaria. For example, Beisel and Boëte note that the transfer of genetically modified (GM) mosquitoes from lab to field, potentially including GDOs in future, “also involves a transfer from North to South, from laboratories in high-tech knowledge economies to (often) resource-poor developing countries” (Beisel and Boëte 2013, 47).

In wealthy OECD countries, the idea of the knowledge-based economy has become a key driver of research investment. The ‘knowledge’ embedded in a product is seen as adding value to it. Compared to physical goods, knowledge is less tangible and hence more difficult to value, trade and control. Thus, industries depending on knowledge want to pin it down and build walls around their own knowledge, in order to control and protect it from competitors. Intellectual property rights became these walls. They give value to this knowledge and allow it to be traded rather than freely used (Gold et al. 2008, 17).

With the general decline in public structural funding during the last decades, universities have experienced increasing pressure to diversify their

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1 The term ‘knowledge-based economy’ (KBE) was first coined by the Organisation of Economic Co-operation and Development (OECD) in a 1996 report which argued that the OECD economies were increasingly based on knowledge, information and technological innovations, underpinned by scientific research and development and patents (OECD, 1996).
financial sources and to rely more on competitive funds (Geuna and Nesta 2006, 791). In theory, patents act as a reward for invention that is supposed to stimulate investment, creativity and economic growth. While originally inventions made with public funding in the USA belonged to the federal government, the adoption of the Bayh-Dole Act in 1980 made it possible for universities to own and commercialise publicly-funded, in-house inventions, and to license their intellectual property to private firms (see Section 6.1, Box 2) (Tofano, Wiechers, and Cook-Deegan 2006, 54). With this change in policy, which has since been copied elsewhere in the world, huge amounts of private capital have been invested in certain types of R&D. As a result, researchers started to think about commercial uses of their work and pressure to file patents rose, with some researchers even being bound by contract to tell their funders about any invention that could be patented and commercialised (Tofano, Wiechers, and Cook-Deegan 2006, 57).

In this context, it is not surprising that ‘hype’, or exaggerated promises about valuable future commercial applications and social benefits, started to appear in scientific research studies, in an effort to help secure research funding. Additional issues arising from this development relate to conflicts of interest and transparency; for example, ties to industry and the incentive to patent may be problematic for the independence and autonomy of researchers (Geuna and Nesta 2006, 796). Patent applications are often not declared in scientific papers (Mayer 2006). Scientists who are named as inventors on patents will in some cases have a direct financial interest in promoting the claims of ‘industrial applicability’ made in the patent. In other cases, the patent may not confer a direct financial reward, but defending the claims made in it may still be important for the scientist’s career and future funding.

Biotechnology is an important part of this fundamental change to science. For example, Joly notes that the privatisation of agricultural research and development is related to economic policies and to reductionism in science, i.e. to “the promises associated with the biotechnology revolution, and specifically the ‘molecularisation’ of life sciences, which prompted major changes in research and development (from the experimental field to the research laboratory, increasingly disciplinary and reductionist research and development, concentration of research in a small number of institutions), and the patentability of life forms…” (Joly 2005, 619).

Commercial biotechnology emerged at the same time as the above-mentioned change to US and international patent policy (Tofano, Wiechers, and Cook-Deegan 2006, 54). Biotechnology became a business when the knowledge emerging from scientific research became classified as intellectual property (IP) that was valued and could be bought and sold (Pisano 2006). Many countries followed suit and brought their IP laws in line with those of the US, in order to benefit from the biotechnology boom (Gold et al. 2008). A watershed moment was when venture capitalists learned that IP could be bought and sold independently of the final product (Pisano 2006, 142). This has allowed hype around new technologies to influence both public and private R&D investments, and allowed money to be made from simple promises, even when useful final products are often not delivered and when there is no net benefit to society or the economy.

More recently, philanthropic donations have begun to play an increasing role in the research and development of new technologies, for example in the case of GM mosquitoes, including those with gene drive. Thus, Beisel and Boëte argue that “GM mosquitoes render the mosquitoes themselves as a commercial product; a commercial product in a political economy funded by philanthropic initiatives, shaped by private university spin-offs and characterized through economic inequalities” (Beisel and Boëte 2013, 54).
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3 Funding for Gene Drive research and development

The biggest investments into gene drive research and development (R&D) come from the US military, large philanthropic donors and government-funded research agencies. In the following sections, we will look at who the main gene drive funders are, what they are funding and how this may be relevant for public engagement exercises.

3.1 Military and intelligence agencies

The U.S. Defence Advanced Research Projects Agency (DARPA) announced in 2017 that it will invest $65 million over four years in the ‘Safe Genes’ programme that funds seven major research projects focusing on gene drive and genome editing R&D. (DARPA 2017). The Gene Drive Files, a trove of documents and emails obtained by civil society investigators through a Freedom of Information request, reveal that the total amount DARPA invests into the ‘Safe Genes’ programme is $100 million, likely making them the largest single funder of gene drive R&D (Gene Drive Files 2017a, 1). One of the ‘Safe Genes’ projects, led by Keith Joung at the Massachusetts General Hospital, receives $11 million from DARPA, and part of the project funding goes to Target Malaria investigators, at Imperial College in London. The team at Imperial College for the first time achieved complete population suppression of caged mosquitoes using gene drives (Kyrour et al. 2018). That research was funded not just by DARPA, but by the Bill & Melinda Gates Foundation and the UK Biotechnology and Biological Sciences Research Council (BBSRC) as well (Kyrour et al. 2018, 1066).

Other military and intelligence organisations involved in gene drive R&D are the Intelligence Advanced Research Projects Activity (IARPA) and the US Army Corps of Engineers (ACE) (Gene Drive Files 2017b).

3.2 Philanthropic foundations

The Bill and Melinda Gates Foundation (BMGF), the largest philanthropic foundation in the world (Belluz 2015), has long had a leading role in funding GM mosquito research (Enserink 2010). Beisel and Boëte (2013, 47) note that: “Before the establishment of the Gates Foundation, research on genetic manipulation of insects was a small niche field...” They also highlight how one of the foundation’s strategic aims now focuses explicitly on developing insect technologies, thus accelerating the development and testing of GM mosquitoes. BMGF provides the core funding, $75 million so far, for the Target Malaria project (Regalado 2016a). Target Malaria is a research consortium that aims to control the spread of malaria by releasing genetically modified gene drive mosquitoes. Target Malaria has progressed R&D on gene drive mosquitoes further than other groups and is currently operating in Burkina Faso, Mali and Uganda (Target Malaria n.d.a).

The Open Philanthropy Project (OPP), whose major funders are the couple Cari Tuna and Dustin Moskovitz (co-founder of Facebook and Asana), is another major philanthropic donor that has awarded an additional $17.5 million to Target Malaria (Dunning 2017). OPP has also awarded $1.2 million to the Foundation of the National Institutes of Health (FNIH) to form a working group of approximately twenty experts tasked with developing a consensus pathway for field-testing gene drive mosquitoes (Open Philanthropy Project 2016).

The FNIH itself is another key actor supporting the development of gene drives. In collaboration, again with the Bill and Melinda Gates Foundation, along with numerous research institutions around the world, the FNIH managed the Vector-based Control of Transmission: Discovery Research (VCTR) programme (Foundation for the National Institutes of Health n.d.). The VCTR programme supported Target Malaria’s R&D on gene drive mosqui-
tos (see for example Eckhoff et al. 2017, E264 and Hammond et al. 2016, 82).

In addition to the funding from such philanthropic organisations, Target Malaria has also received direct governmental funding from the European Commission, the UK Department of Environment, Food and Rural Affairs (DEFRA) and the Ugandan Ministry of Health (Target Malaria n.d.b).

Tata Trusts are among the top philanthropic organisations in India and have awarded $70 million to create the Tata Institute for Active Genetics and Society (TIAGS), in collaboration with the University of California, San Diego (UCSD). UCSD announced they would match the trust’s award with a further $70 million. The institute aims to develop mosquitoes that are unable to propagate malarial parasites using gene drives (Philanthropy News Digest 2016).

Other philanthropic organisations that fund gene drive R&D include, among others, the Wellcome Trust (UK), the Burroughs Wellcome Fund (US), the Rainwater Foundation (US), the Greenwall Foundation (US), the Alfred P Sloan Foundation (US), the WM Keck Foundation (US), the Pew Charitable Trusts (US), the David and Lucile Packard Foundation (US) and the Paul G. Allen Frontiers Group (US) (Esvelt 2018a, 8; Gantz et al. 2015, E6742; Grunwald et al. 2019, 109; Sculpting Evolution n.d.a; Target Malaria n.d.b).

3.3 Governmental science and research agencies

The Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO) is a partner in the DARPA-funded ‘Safe Genes’ project that aims to develop and test a mammalian gene drive system in rodents (Godwin 2017). According to the Sydney Morning Herald, CSIRO has allocated $3.5 million for “community research related to synthetic biology” to secure “social licence” for its gene drive ambitions (Wilson 2018). The goal of this social engagement seems be securing social acceptance, rather than fostering true democratic decision-making (see Section 10). According to an email obtained by a Freedom of Information request, CSIRO has also been promoting the rodent gene drive technology to various government agencies and other stakeholders (Wilson 2018).

Furthermore, the UK Biotechnology and Biological Sciences Research Council (BBSRC) is funding mouse and rat gene drive research at the Roslin Institute at the University of Edinburgh as well as mosquito gene drive research at Imperial College (BBSRC 2017; Kyrou et al. 2018, 1066).

The US National Institutes of Health (NIH) awarded $1.5 million to Kevin Esvelt for the development of ‘daisy’ gene drives (National Institutes of Health 2017; Sculpting Evolution n.d.a). With support from DARPA and the Bill & Melinda Gates Foundation, NIH and FNIH sponsored the National Academies of Sciences, Engineering, and Medicine (NASEM) gene drive report “Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values” (2016), that intended to “…create a consensus committee to summarize current understanding of the scientific discoveries related to gene drives and their accompanying ethical, legal, and social implications” (National Academies of Sciences, Engineering, and Medicine [NASEM] 2016, viii & 1). NIH further support Target Malaria (Target Malaria n.d.b) and various gene drive studies (see for example DiCarlo et al. 2015, 12; Gantz et al. 2015, E6742; Gantz and Bier 2015, 444; Grunwald et al. 2019, 109).

Other governmental science and research agencies involved in gene drive funding include the Uganda National Council for Science and Technology (UNCST) (Target Malaria n.d.b) and the National Science Foundation (NSC) (see for example DiCarlo et al. 2015, 12; Dhole et al. 2017, 806; Min et al. 2018, S60).

3.4 Guiding principles for the sponsors and supporters of Gene Drive research

As a response to the US National Academies of Science, Engineering and Medicine Report that provided recommendations directed at researchers,
funders and policy-makers (NASEM 2016, 106, 128, 142, 170-172, 177-178), Emerson et al. (2017, 1136) published five guiding principles for sponsors and supporters of gene drive research:

1.) advance quality science to promote the public good;
2.) promote stewardship, safety and good governance;
3.) demonstrate transparency and accountability;
4.) engage thoughtfully with affected communities, stakeholders and publics;
5.) foster opportunities to strengthen capacity and education.

These guiding principles have been endorsed by prominent gene drive funders, including the Bill & Melinda Gates Foundation, Tata Trusts and the US FNIH. Such a pledge to ensure safe and responsible gene drive research is laudable; but can we conclude that further development of the technology will always follow these guidelines and be in the best public interest? Boëte (2018) argues that the list of Guiding Principles is a “voluntary undertaken code of ethical and scientific conduct” (Boëte 2018, 18), which is not legally binding. This means that the signatories cannot be held accountable for actions that do not honour the code.

While governmental funding is, at least formally, accountable to the public, philanthropy is still largely free from public accountability mechanisms and democratic control. The Bill and Melinda Gates Foundation, for example, is only accountable to its three main trustees, that is, Bill and Melinda Gates, alongside Warren Buffet. Although philanthropic and charitable organisations, by definition, aim to serve the public interest, foundation trustees are the ones to decide a.) what the public interest is (e.g. global health), b.) what a problem is (e.g. malaria), and c.) how they want to fix it (e.g. with gene drives) (Barkan 2013).

Today, more and more funders have preconceived notions about social problems and their solutions. In an approach called “strategic philanthropy”, they develop specific policy or outcome agendas to be fulfilled by their grantees; thereafter, the grantees seem to take on the role of contractors (Rourke 2014, 2). Academic experts have questioned the Bill and Melinda Gates Foundation’s global health research priorities. Some in particular critique the emphasis on technology and technological fixes (Belluz 2015). The growing influence wealthy philanthropic organisations, such as the Bill and Melinda Gates Foundation, have on funding for global health (Belluz 2015) and the lack of real public accountability, raises the question of whether, and how, the public can be truly involved in the discourse on gene drive R&D.

As the Gene Drive Files have revealed, the principle on transparency, which is key to the guiding principles, has already been violated by important signatories. They have been officially named as having engaged in coordinated “closed door” efforts to influence UN agencies’ support of gene drives, and also in avoiding media engagement (Boëte 2018; Gene Drive Files 2017c). This gives the impression that instead of genuine stakeholder engagement, which could theoretically result in the rejection of the gene drive approach, the aim of these signatories is simply to gain acceptance for their agenda.

Another issue is that DARPA, as probably the largest funder of gene drive R&D, is missing from the list of signatories. There seems little interest on the part of DARPA to engage thoughtfully with stakeholders and the public in discourse on gene drive R&D. At the first public meeting of the Committee on Gene Drive Research in Non-Human Organisms, Col. Daniel Wattendorf stated: “…we may not have the time in this case to actually wait for, and make calls for, certain scientific actions and communities to deliberate. We actually may need to be working on technology solutions right now. And the alacrity of our [DARPA] institution to be able to do that is at hand” (Wattendorf 2015).

Lastly, while the five guiding principles could become very important for responsible R&D, they currently do not allow for discussion about how a problem should be tackled and what research is
being done in the first place. As we discuss under consideration of the Precautionary Principle (PP) later (Section 8), and as the European Environment Agency has noted, thorough practice of the PP would always include inter alia assessment of what may be the multiple alternative trajectories which could meet the same social goals and needs as the prevailing trajectory. Thus, even a thorough enactment of the five guiding principles would fail to meet the internationally established Precautionary Principle requirements.

4 Conflicts of interest in science

Conflicts of interest may play a major role in what is communicated about a technology, what research is conducted, and how the results of scientific studies are communicated and used in practical investment and regulatory decisions.

It is well established that commercial conflicts of interest in science can jeopardise the independence of research. The discussions in this area have focused on the field of medicine, where compromises have repeatedly occurred in research participants’ well-being, research initiatives, publication of results, interpretation of research data, and scientific advancement, all because of industry funding for research (Tereskerz et al. 2009). Industry funding can also skew the research agenda, with major implications for what kind of research gets funded and how this is communicated and used (Wallace 2009). Adverse effects, among many others, may include biasing the research and associated policy agendas towards false or ineffective solutions to a problem, potentially leading to major negative impacts on public health (Wallace 2009; Kearns 2016).

Conflicts of interest are not limited to scientists working in the commercial sector. Krimsky (2003) describes how university science is now entangled with entrepreneurship, and investigates the effects of modern, commercialised academic science. Vallas and Kleinman describe how “the structural reconfiguration of academic science generates an increasing tension between the ‘ideal’ culture of academic science and the ‘real’ culture of market-oriented logics governing the pursuit of capital in one or another form” (Vallas and Kleinman 2008, 306). Patents held by academic scientists are also a recognised source of conflicts of interest (Mayer 2006). In relation to GDOs, Brossard et al. note that “relevant conflicts of interest can go beyond the financial ones and can include how the topic at hand relates to our worldviews, the success of our next grant proposal, or the positive views of our administrators and colleagues” (Brossard et al. 2019, 5).

In addition, bias is not limited to commercial interests. Scientific bias has been well studied in the medical research literature, where several types of interpretative bias (bias in the analysis of data, rather than in the measurements themselves) have been identified (Kaptchuk 2003). These also include “confirmation bias” – evaluating evidence that supports the scientist’s preconceptions differently from any evidence that challenges these convictions (Kaptchuk 2003, 1454).

A major problem is scientists ‘over-promising’ in order to secure research funding, which is now almost routine (Gannon 2007). Hype and ‘over-promising’ are discussed further below. Other impacts of conflicts of interest in GM insect research are discussed further in Section 7.
5 The role of hype in the Gene Drive discussion

5.1 The role of hype in securing research funding (for Gene Drive research)

Hyperbole or “hype”, in terms of scientific research, means “extravagant or exaggerated promotion” of whatever one protagonist is attempting to sell to another. Promises about future benefits play an important role in securing (competitive) investments in R&D. In some cases, the grant being sought is corporate or venture capital investment, underpinned by intellectual property (IP). In other cases, funding for research, whether academic or private, may be coming from governments, philanthropic organisations or a combination of the above.

Writing more than a decade ago, Gannon (2007) argues that “hype” in science is spreading for several reasons, including: the increasing pressure on institutions and researchers to secure funding from diverse sources; the requirement that scientists explain the relevance of their work to the general public; and the fact that many grant applications require the applicant to explain the impact of their work on society. Scientists are in a fierce competition to maintain and increase public as well as private support and funding, and therefore, “...scientists over-promise by sending messages of being close to their goals, even if this is not true” (Gannon 2007, 1087). Gannon notes that the promise that a cure is just around the corner, if only a few million more in funding is forthcoming, more often than not is an exaggeration. However, when it comes to scientific publications and grant applications, reviewers do not usually comment on the credibility of the claims made for future benefits that might arise from the research. Furthermore, they do not ask for the same level of proof for these speculations as they do, for example, for speculations on a step in scientific methods. This has led to overstretched expectations of what science and technology can achieve, both among the public and among funders.

Future releases of GDOs have been claimed to bring tremendous benefits to society, for example the end of malaria or Lyme disease. Even though R&D is still in its infancy and far from any field trials, gene drive researchers have informed potential philanthropic funders that “gene drive research has the potential to make enormous positive impacts on global human health” (Darrow et al. 2016, 3). Whilst this recommendation comes with extensive caveats about the need to also fund “gene drive safety and control”, little doubt is expressed about the ability of open releases of GDOs soon being able to play a major future role in tackling serious infectious diseases. In some academic journals, in contrast, numerous doubts are expressed about the potential of GDOs to deliver on any of these promises.

One issue is the likely evolution of resistance to the introduced trait. For example, Brossard et al. note that most of the public discussions of gene drives relate to one type of gene drive, where the release of a small number of individuals could, in theory, cause the spread of the gene drive through entire populations of the engineered species worldwide. They state that “It is important to recognize that this is only one type of gene drive and that it will be very difficult to develop such a gene drive to function indefinitely without pests evolving resistance to it” (Brossard 2019, 2). They also note that an alternative approach involves the use of a GDO which produces many unviable offspring; but this would theoretically require enough individuals to be released so that the engineered individuals are initially more than 25% of the total population. In practice, there might be significant practical difficulties in achieving this, in addition to the complexities of how ecosystems might respond.

In relation to GM mosquitoes, including those incorporating gene drive mechanisms, Beisel and Boëte ask “How might a control strategy that is embodied in the mosquito genome play out in the...
face of ecological complexity, adaptability and resistance? Which risks might the strategy entail and how are risks and benefits distributed?” (Beisel and Boëte 2013, 40). They also raise the question of “how to think about biological adaptability of GM mosquitoes in relation to the coexistence of mosquitoes, parasites and humans over time?” (Beisel and Boëte 2013, 42). The same authors also note that the basic relationship between the density of mosquitoes, human infection and disease is poorly understood. More than 450 species of *Anopheles* mosquitoes are known worldwide; around 70 are malaria vectors (of which 41 are thought to be dominant vector species or species complexes), and the rapid reproduction and evolution of mosquito populations makes them dynamic and adaptable (Beisel and Boëte 2013, 46; Sinka et al. 2012, 1). Moreover, new species continue to be identified with the aid of molecular techniques (Coetzee et al. 2013). Hybridisation occurs between major vector species, with hybrids typically occurring at rates of about 1% in most areas, but up to 24% in others, for reasons that are not fully understood (Lee et al. 2013; Mancini et al. 2015). This poses a risk of gene flow between species, if gene drive *Anopheles* mosquitoes were to be released. However, the fact that hybridisation is limited also implies that releasing one species of gene drive mosquito is unlikely to suppress the population of another species, which may therefore expand its range and continue to transmit malaria. This multi-species challenge is rarely discussed in public.

### 5.2 The role of hype in framing the public discourse

Public support is a very important factor contributing to the success of a technology and its capacity to become economically viable (Esvelt 2018a, 5). Since the 1990s, when there were major concerns amongst policy, commercial and scientific elites about indiscriminate public mistrust in science, cultivation of public acceptance of science-based innovation of almost any kind has become a policy and industrial mantra. For example, the perceived worth and benefit of potential applications have always played an important role in public acceptance of biotechnology. “The relatively low levels of public support for a variety of gene transfers change dramatically when a gene transfer is tied to achieving a specific goal that is deemed worthy” (Amin et al. 2007, 42).

Media, including scientific media, often over-emphasise the potential future benefits of any given technology while downplaying the risks. While the media’s desire to tell an interesting story may be partially responsible for reporting exaggerated promises, journalists are not always the source of such exaggerated claims. Bubela and Caulfield (2004, 1399) found that the majority of 627 analysed newspaper articles accurately reflected the claims made in scientific and medical journals. Although media sources can be at fault as well, pressure by industry and funding entities may lead researchers to make claims about future benefits of gene drives in order to secure research funding. Picked up by media journalists, these claims may then also frame public understanding of the technology and what it might do long before it is ready to be applied. In the end, it is important to note that researchers, media and industry all play a role in framing the public discourse of gene drives.

In the following sections, we will have a closer look at some examples of exaggerated and overly optimistic promises made about this technology in newspaper articles, as well as in scientific journal articles and patent applications; and we will discuss how erroneous descriptions and perceptions contribute to framing the public discourse.

#### 5.2.1 Headlines

Headlines are a source of information for the many people who do not have the time to read full articles. Of course, headlines tend to exaggerate and use catch-phrases in order to gain the reader’s attention. Gene drive-related headlines often include exaggerated and sometimes quite unsubstantiated promises, for example making claims about being able to offer public health or conservation benefits.
• The CRISPR machines that can wipe out entire species (Ryan 2019).

• Argument builds around a genetic tool that can erase an annoying species (Meador 2016).

• Genetically modifying Zika virus out of existence (Flam 2016).

• Powerful ‘Gene Drive’ Can Quickly Change an Entire Species (Stein 2015).

Since to date no open releases of gene drive organisms have taken place (nor are such releases planned), it is too early to say what GDOs “can” do, or that they will be able to predictably wipe out a species. The gene drive research currently being done is lab and modelling work. As Oxitec’s failed open release experiments with GM mosquitoes in the Cayman Islands have shown (GeneWatch UK 2018), results from the lab or models can be insufficient predictors what will happen in the field. However, much confidence was invested by the scientists in those partial methods. Using a headline that strongly implies what the technology can do once ready to be applied may be less of an informative description and more of a mechanism for influencing public understanding of the technology.

5.2.2 Terminology

In a subtler way, the language and terms used to describe gene drives can themselves convey promises which influence how the technology is perceived. Different terms are being used to portray what gene drives are supposed to be able to do: modification drive, suppression drive, sensitising drive, global drive, local drive or daisy chain gene drive, reverse drive or daisy restoration drives, etc. Some of these terms, especially “local drive” or “reverse drive”, intentionally convey a promise of safety, containment, control, reversibility and redress, even though none of these concepts has ever been proven. Kevin Esvelt has often publicly stated that he opposes closed-door science and that gene drive research must be open and transparent (see for example Esvelt 2016; 2018b). Therefore, he wants to inform the public about the experiments his research group is planning to do before they are actually conducted. As a result, before actually successfully developing them, Esvelt’s ‘Sculpting Evolution’ research group has presented its concept of so-called ‘daisy chain gene drives’ and what different versions could do. By doing so, they helped to establish many of the above-named terms, although all are hypothetical. Not only do we not know whether these theoretical concepts will behave as intended and promised in the field, they have not even been demonstrated in a lab.

Nevertheless, many speculations have already been made, for example: that the daisy drive system will “return power to the hands of local communities” (Sculpting Evolution n.d.b), who, once (and if) it is operational, will be able to decide whether or not to use gene drives to solve local ecological problems; or that they could be used to restore a population to its original genetic state (Sculpting Evolution n.d.c). While these researchers find it problematic to release GDOs that are designed to “spread indefinitely” (Sculpting Evolution n.d.b.), they see no problem in releasing daisy drives, which are intended to have a limit to their spread. In their patent application on daisy chain gene drives (see Section 6.2) they promise: “Daisy chain gene drives designed using methods provided herein can be used to address otherwise intractable ecological problems, with a level of safety inherent in their design, that reduces or eliminates a likelihood of global effects as occurs for conventional gene drive organisms that are released into the wild”, and: “Unlike previous global gene drive system, methods of the invention provide designs for daisy chain gene drives that can be safely tested in field trials” (Esvelt, Min, and Noble 2017, 55-56).

A side-effect of this supposed open and transparent approach to research is that a.) promises about future benefits of a hypothetical, untested concept are made very early in development; b.) the language and terms conveying these promises, as if they were already-proven reality, are already established in society well before a technology actually exists.
5.2.3 Application promises

As discussed above, a specific goal or application perceived perhaps as dangerous but also as worthy, for example in saving human lives, can increase public support for that technology. Therefore, it is important to show the public how they personally, or the world as a whole, can directly benefit from this technology: “Although many questions about this technology remain unanswered, we are optimistic about the potential of gene drives in strengthening the public health arsenal and reducing worldwide human suffering” (Darrow et al. 2016, 2).

Although any form of gene drive technology is far from being tested in the field and further yet from its promises of beneficial applications becoming reality, a lot of emphasis has already been placed on future beneficial applications being delivered once the technology is made available. For example, the following quotes paint an overoptimistic picture of the potential health, environmental and agricultural applications of gene drives: “The ability to edit populations of sexual species would offer substantial benefits to humanity and the environment. For example, RNA-guided gene drives could potentially prevent the spread of disease, support agriculture by reversing pesticide and herbicide resistance in insects and weeds, and control damaging invasive species” (Esvelt et al. 2014, 1); “…it could be used to conserve threatened or endangered species, combat invasive species, or control agricultural pests. It is particularly tantalizing as a potential weapon against vector-borne infectious disease” (Abbasi 2016, 483); “Effective gene drives may enable us to control invasive species, re-sensitize organisms that have developed resistance to insecticides and herbicides, and reduce or eliminate many types of vector-borne diseases, all at a low cost“ (Champer, Buchman, and Akbari 2016, 147).

As the examples above show, three areas of applications of gene drives are most prominent: public health, conservation and agricultural applications, with hoped-for eradication of vector-borne diseases currently being the most commonly hyped potential application of gene drives. In addition to these direct benefits promises about the results of gene drive R&D, it is sometimes argued that the gene drive approach might actually be the more sustainable alternative for other already applied technical solutions, for example by decreasing the numbers of GM mosquito releases: “To date, trials [with GM mosquitoes] have used a self-limiting approach, requiring repeated mass release of GM males. But a self-sustaining control would be possible using a gene drive system, eliminating the need for ongoing releases…” (Piaggio et al. 2017, 102); or by decreasing the use of toxic pesticides: “For example, a gene drive to suppress non-native rodent populations on remote islands could reduce the need for alternative forms of control such as the use of rodenticides. The cost of administering rodenticides is estimated to be in the millions of dollars and rodenticides may also harm non-target species” (NASEM 2016, 5). Not mentioned is the question of whether gene drives will work in mammals at all, and what practical and social implications the release of gene drive rodents on these islands might have: for example, how many GDOs would have to be released to efficiently control the island population, how long would that take and what damage could the GDOs cause in the meantime?

Furthermore, it has even been argued that Gene Drives “could make the world a more just place”, thereby adding a moral, ethical component. According to the MIT technology review, Esvelt considers evolution a blind, amoral process, whose only goal is to survive, comparing it to a “larger failing of the universe”. This should be rectified with gene drives and the ability of experts like himself to “fine-tune the battle for survival” (Regalado, 2016b). This shows the immense confidence of some gene drive researchers that they are not only able to alter organisms and eventually populations, but the evolutionary process itself. Fittingly, Esvelt called his research group at the MIT media lab in Massachusetts “Sculpting Evolution”.

Below we will take a closer look at the specific promises made in these three sectors.
Public health promises

Where biotechnology is concerned, human medical and health applications are generally better accepted by the public than are agricultural applications (Amin et al. 2007, 40). In the gene drive discourse, a great deal of emphasis is being put on potential public health benefits. The most common promise is that gene drives, once applied, will have the potential to eradicate vector-borne diseases such as malaria, dengue fever or Zika, either by suppression of the vector population or by rendering the vector population resistant to the parasite, virus or bacteria. This is illustrated with the following quotes: “With gene drives, it may be possible to kill off a mosquito population or make the population resistant to malaria parasites” (Wade 2015a); “Gene Drive mosquitoes have tremendous potential to help eliminate malaria, and multiple gene drive approaches have recently shown promise in laboratory settings” (Eckhoff et al. 2016, E255); “These findings could expedite the development of gene drives to suppress mosquito populations to levels that do not support malaria transmission” (Hammond et al. 2016, 78); “In the U.S., scientists are racing to develop similar genetic suicide vests for mosquitoes that spread Zika and dengue fever” (Regalado 2016b).

When gene drives are proposed as potential solutions for public health concerns, the proponents build their narrative by citing the large numbers of people suffering and dying each year from specific illnesses: “Malaria alone kills over 650,000 people each year, most of them children, while afflicting 200 million more with debilitating fevers that economically devastate their societies. Dengue, yellow fever, trypanosomiasis, leishmaniasis, Chagas disease, and Lyme disease are caused by other pathogens that spread using vectors. All of these can potentially be reduced or even eliminated by driving changes in the vector that prevent transmission” (Esvelt and Smidler 2015, 28-29); “A large region, at least in principle, could be freed from malaria, which kills almost 600,000 people a year” (Wade 2015b).

Sometimes the promises are highly specific and ambitious: “Such genes, if successfully propelled throughout a wild mosquito population, would render a region free of the malarial parasite, which could no longer spread via mosquito bites” (Wade 2015a); “the inserted genes are expected to spread rapidly and take over a wild population in as few as 10 generations, or a single season” (Wade 2015b, emphasis added). Another, equally optimistic one states: “Although all vector species must be targeted in a given area in order to stop transmission, the disease will be permanently eradicated if the newly vacated ecological niches are filled by competing non-vector species. Significantly, this strategy requires little or no understanding of the vector’s molecular biology, but unavoidably entails the local or possibly global extinction of the vector species” (Esvelt and Smidler 2015, 29, emphasis added).

Such statements convey the impression that once this technology is applied, it will work predictably, as intended, and also that it will work rapidly, thereby being a sensible or the only solution to combat vector-borne diseases. Missing are all the varied caveats about what might go wrong if the technology doesn’t work as intended; for example, when the mosquitoes develop resistance to the gene drive.

Anyone conversant with biology knows that there is no guarantee that the vacated ecological niche will be filled with a non-vector species, as Esvelt and Smidler (2015) suggest, and not by another mosquito species (Wilke et al. 2018, 5-7). Furthermore, potential ecological problems arising if an ecological niche is filled with a species that previously played a minor role in that particular ecosystem are not brought up. In the case of genetically modified Bt crops, we have seen that reducing the numbers of a specific pest in an area often leads to the establishment of secondary pests that may be just as destructive (Lu et al. 2010; Wang et al. 2008; Wu et al. 2002; Zhao 2011). In the case of mosquitoes which transmit dengue, the former Chief Scientific Officer of GM insect company Oxitec, Luke Alphney, has stated: “Since Ae. aegypti and Aedes albopictus are known to compete…it is possible that the successful implementation of...gene drives could lead..."
an existing *Ae. aegypti* population to be displaced by *Ae. albopictus* where it would not otherwise have been. This would likely hamper efforts to eliminate viruses such as dengue since *Ae. albopictus* are also competent vectors...” (Edgington & Alphey 2018, 21-22).

**Conservation promises**

It is often promised that synthetic biology and especially gene drives could make a significant contribution to conservation efforts. In 2017, Piaggio et al. published a paper called “Is it Time for Synthetic Biodiversity Conservation?” in which they claim that synthetic biology might be the long-desired solution for many conservation problems. They state: “The field of synthetic biology, which is capable of altering natural genomes with extremely precise editing, might offer the potential to resolve some intractable conservation problems...”, adding: “It has become apparent that synthetic biology holds tremendous potential across numerous fields, including conservation biology” (Piaggio et al. 2017, 97).

One promise often mentioned is that gene drives could help control invasive alien species, such as rodents on islands, resulting in protection for the endangered species threatened by them. Although this is highly theoretical and far from any experimental validation, gene drives are already being treated by some science reporters and gene drive researchers as known working tools in the conservation toolbox: “What’s more, the technology also offers a new way to delete invasive species from islands like Hawaii, something that could rescue native birds at the edge of extinction” (Regalado 2016b). As seen above with promises about public health, proposals to use gene drives as solutions often portray the severity of the situation and then propose gene drives as potential technical fixes, without appropriate time or research going into whether they will work as intended, what could go wrong on the ground, how we would deal with that and especially, what the alternatives are: “One of the most environmentally damaging consequences of global economic activity is the transport of invasive species, which often causes ecological disruption and the extinction of native species. Isolated ecosystems such as those on small islands are especially vulnerable. Cas9 Y-drives have tremendous potential to promote biodiversity by controlling or even eradicating these species from individual islands or possibly entire continents” (Esvelt and Smidler 2015, 29).

Another promise is that gene drives could immunise endangered species, such as amphibians, against pathogens: “Although not yet developed, other payload genes of great practical importance may immunize threatened or agriculturally important organisms against pathogens, such as...genes that render amphibians immune to the killer Chytrid fungus, which is responsible for the decline of amphibian species all over the world” (Champer, Buchman, and Akbari 2016, 147) or “Such RNA guided Cas9 gene drives may be used to quickly spread protective alleles through threatened or soon-to-be-threatened species such as amphibians” (Esvelt and Smidler 2015, 28).

The extremely speculative nature of such statements is rarely highlighted, and readers (the public and the funding bodies) are likely to infer the scientists’ excitement and confidence reflects imminent breakthroughs, rather than what is more likely, a desire for public approval and further funding. Statements about the practical implementation of these approaches are mostly lacking. Grunwald et al. (2019), for example, indicate that there might be additional technical hurdles to develop efficient gene drives in mammals, compared to insects, stating “…it appears that both the optimism and concerns [that gene drives could be used to reduce invasive rodent populations] are likely to be premature” (Grunwald et al. 2019, 108). Moreover, alternative methods to control invasive species that are, or with better understanding, could be available to society, may be equally cost-effective and much more within the realm of predictability and control than these as yet non-existent technical fixes. But this basic dimension of responsible democratic social appraisal and choice seems largely ignored. Gene drives are portrayed as an added or even only possible solution to different conservational issues in the above mentioned statements, although many of the species mentioned have never even been tested in the lab.
Agricultural promises

Gene drive patent applications also include many potential agricultural applications. In his 2003 patent application, Burt already stipulated that gene drives could be used to control pest populations or to render pest and weeds that have developed resistances to certain pesticides susceptible again, stating: “The method may also be used to interrupt other, non-lethal genes, e.g. a gene that confers a pesticide resistance onto a crop, thus making the pest susceptible to the pesticide again” (Burt 2003, 31). Nevertheless, agricultural applications, such as gene-drive mediated pest control, are less widely discussed in the media than potential health or conservation related applications (Courtier-Orgogozo et al. 2017, 878). As stated above, human medical and health applications are generally better accepted by the public than agricultural biotech applications. Potential agricultural applications being mentioned – mostly gene drive-mediated pest control, or the reversal of pesticide resistance, using so-called “sensitising drives” - are portrayed as sensible or sustainable solutions to current agricultural problems: “Additionally, the versatility of RNA-guided endonucleases may allow for other suppression approaches, such as the reversal of resistance to pesticides or herbicides by specifically targeting resistance alleles and replacing them with sensitive ones — a process that could be repeated if resistance is reacquired” (Champer, Buchman, and Akbari 2016, 147), or: “Compared to other pest management techniques, it [gene drive-mediated pest control] is cheaper, more precise, and, so far, less controversial as, say, the use of pesticides”, adding that gene drive-mediated pest control may “easily eradicate a species” (Courtier-Orgogozo et al. 2017, 878). However, these are still approaches within the prevalent industrial agricultural system, likely to be attractive to major agrochemical companies (further discussed in Section 6.2). Moreover, gene drives so far have not been tested and might not work in plants. For example, the cell repair mechanism predominant in plants might prevent the gene drive element to be copied to the damaged chromosome (see Chapter 1 for more details). As for other GDOs, ecosystem responses may also be complex and unpredictable.

5.3 Implications of hype for alternatives

Hype about new technologies can undermine existing or more practicable alternatives, by diverting resources from promising approaches. For example, Beisel and Boëte note that “beyond the question of whether or not GM mosquitoes can work, we should be asking what other kinds of techniques they replace or marginalize by directing resources away. As a tool of transfer and an instrument of eradication, they entangle malaria in institutional and economic calculations—between companies, philanthro-capitalist endeavours, macroeconomic models and global health agendas. At the same time, GM mosquitoes disentangle malaria from more local forms of control—the low-tech labour-intensive forms of management that belong to place” (Beisel and Boëte 2013, 47).

However, the body organising public engagement in new technologies is often the same one that has developed and/or invested in the technological fix being promoted. As such, it does not have proper incentives to explore alternatives as part of any public engagement exercise. Although alternatives are often mentioned, this is usually in a way which highlights their limitations and diminishes or dismisses the role that they can play. In the agricultural GM crops domain, Vanloqueren and Baret (2009) have explained in detail how this anti-scientific lock-in to a particular technology occurs, and how it correspondingly locks out what may well be more sustainable, more ethical, and more acceptable, alternative technical, scientific and social trajectories.

For example, for dengue control, the GM mosquito company Oxitec restricts discussion of alternatives to GM mosquitoes to the use of larvicides and adult spraying, with most focus on adult spraying (which is widely recognised to be ineffective), although they do mention wearing a long-sleeved shirt and using mosquito repellent (Parry 2012).
They do not discuss existing methods of control, such as destruction of breeding sites by government-employed inspectors or local communities; or social and environmental measures, such as improving water and sewage systems and shredding waste tyres (which provide potential breeding sites). Absence of a tap water supply is correlated with an increased incidence of dengue, because water storage containers used by households without tap water supply provide mosquito breeding sites (Schmidt 2011, 6), and the presence of a good primary health care system can significantly reduce the incidence of dengue (Roriz-Cruz et al. 2010). World Health Organization research has also focused on utilising new non-insecticidal intervention tools (such as rectangular water container covers in India, sweeping nets or dragon fly nymphs in Myanmar, and copepods and screen covers for earthen jars in Thailand), and on engaging local communities in these methods (TDR 2013).

Reis de Castro and Hendrickx (2013, 121) use the concept of ‘ordinary treasure’ to describe how releases of Oxitec’s GM mosquitoes in Brazil were characterised as both ordinary (and hence unproblematic) on the one hand, and as valuable treasures (embedding hopes and expectations of tackling disease). Reis de Castro and Hendrickx (2013, 123–124) describe a ‘rhetoric of hope’, in which arguments about the possible negative effects of releasing GM mosquitoes in Brazil are perceived as a threat to the economy, and moreover, in the case of new technologies designed to tackle disease, as equivalent to not caring for people who are suffering. Reis de Castro and Hendrickx note (2013, 123) how the GM insect technique “follows a deep-rooted logic that focuses on the mosquito, rather than analyzing and improving social conditions, health care or medical interventions” and conclude (2013, 124) that “In this sense, the case of the transgenic mosquitoes in Brazil evidences a technological fix that proposes to overcome not only a problem in the individual attitude [to mosquito control] or the government’s actions, but an entire deficient infrastructure”. This analysis raises questions about the wisdom of spending time and money on unproven technology, rather than fixing the social structures that caused the problems in the first place.

The same rhetoric is now evident in claims about GDOs, including the potential use of gene drive in mosquitoes to tackle diseases such as malaria, as detailed above.

Failure to properly include alternatives can lead to significant opportunity costs, especially if large sums of money and other resources, as well as time are wasted on unrealistic future promises rather than implementing existing interventions effectively and conducting more cost-effective, diverse, and appropriate R&D. For example, Beisel and Boète argue that “Funding silver bullet solutions such as GM mosquitoes diverts resources away from more low-cost and local measures in malaria control like mosquito nets, larviciding, or increasing health systems capacities in order to improve access to malaria treatment” (Beisel and Boète 2013, 54).

5.4 Implications of hype in current public engagement exercises

There are no current open releases of gene drive organisms. However, there have been open releases of genetically modified (GM) insects on an experimental scale, conducted by the commercial company Oxitec, which is now owned by the US company Intrexon (Intrexon n.d.). In Burkina Faso, the research consortium Target Malaria aims to begin experimental open releases of GM mosquitoes over the next year, with a view to beginning open releases of gene drive mosquitoes in five to ten years’ time. In the US, MIT researchers are proposing releasing hundreds of thousands of GM mice into the environment of Nantucket Island. This project is also seen as a possible step towards releasing gene drive mice in the future: however, the researchers say they do not intend to build gene drives in this organism until field trials of non-drive mice are completed and local communities request a drive system (Esvelt n.d.). Genetic Biocontrol of Invasive Rodents (GBIRd) is another research consortium, focused on developing gene drive organisms in rodents, with a view to releasing them into the environment to attempt to eradicate pests (GBIRd n.d.).
Since no GDOs have yet been released into the environment, it is worth examining some of the proposals to release GM insects – which have taken place, or are imminent – in order to compare the rhetoric of the relevant institutions with what happens in reality. This is particularly important in the case of Target Malaria, which plans to release GM mosquitoes in the next year, followed by gene drive mosquitoes in 5 to 10 years’ time.

On its website, Oxitec describes its GM Aedes aegypti mosquitoes as “the solution” to the diseases spread by this species of mosquito (including dengue, Zika, chikungunya and yellow fever) (Oxitec n.d.a). In contrast, Wilke et al (2018, 5) note that the ecology of GM mosquitoes is not completely understood, and their supposed interaction with particular biomes and non-target species is mostly theoretical. That’s just one of the reasons why environmental and ecological variations may alter the expected outcome of suppression strategies based on GM mosquito releases, which will possibly result in failure to suppress targeted mosquito vector populations, or in other surprises. Reis de Castro and Hendrickx state, “Even from a ‘technical’ viewpoint it is by no means clear when the mosquito technology can be said to work: does it mean diminishing the prevalence of dengue? To what extent? Does “working” mean suppressing the population of wild mosquitoes – if so, by how much, for how long? Further research will be necessary to see how the mosquitoes are made to work, under what sort of geographical and economic conditions, and with what types of political alliances” (Reis de Castro and Hendrickx 2013, 127).

To date, all Oxitec’s open releases of GM mosquitoes have been experimental; there is no evidence of any reduction in the target diseases; and claims for successful suppression of mosquito populations have been highly exaggerated (GeneWatch UK 2018). Nevertheless, public engagement exercises undertaken by Oxitec take the claimed benefits of open releases of their GM mosquitoes as fully established and undisputed. For example, in Brazil, Oxitec’s public engagement included a jingle claiming that Oxitec’s GM mosquitoes are “the solution” to dengue, “Let him into your house, He’s the solution, He fights dengue and won’t bite anyone, Protect your health, He’s the good mosquito” (Bevins 2012).

In 2018, the Environmental Health Minister in the Cayman Islands confirmed that trials of Oxitec’s GM mosquitoes there did not work and would be abandoned (Cayman News Service 2018). Trials in Panama and Malaysia had already been abandoned by this time, and in Brazil, a totally new version of the technology was undergoing early trials. Thus, this claim that the GM mosquitoes that had already been released were a “solution” was not supported by any evidence.

Similarly, Oxitec’s website describes its GM crop pests as “the solution” to pest control problems involving four different pest species affecting crops such as brassicas, soft and stone fruits, maize, rice, sugarcane, cotton and more than 250 kinds of fruits, nuts and vegetables (Oxitec n.d.b). However, Oxitec has not yet demonstrated that any of their Genetically Modified pests could suppress a wild pest population in the field. Further, the trait engineered into these GM pests is female-killing “late acting lethality”, i.e. the female offspring of the release GM males die mainly at the late-larval or pupal stage (Fu et al. 2007, 354). This raises concerns about the damage they would do to crops during the repeated mass releases that would be needed to attempt to suppress a wild population (Benedict et al. 2010, 26); and about the contamination of crops with GM larvae (many of which may die inside the crop) (Reeves and Phillipson 2017). These issues are likely to limit the practical application of this technology in real-world situations, but are not mentioned in the company’s publicity material.

Target Malaria’s website does not claim it has an existing “solution”, but does say it is aiming to develop one. It states: “Target Malaria is an innovative project aiming to reduce the population of malaria-transmitting mosquitoes in sub-Saharan Africa. By reducing the population of malaria mosquitoes, we aim to reduce the transmission of the disease” (Target Malaria, n.d.c) and “We aim to develop a technology that can be complementary to other mosquito control methods and which of-
fers a solution that is long term, cost-effective and sustainable as it tackles the problem at the source” (Target Malaria n.d.d). Nevertheless, Target Malaria’s technology is excessively promoted considering it is something which does not yet exist in a form even close to being ready for experimental release, even in the lab. On the BBC in October 2018, one of the project’s researchers stated that “The benefits that this technology can have in terms of human lives is massive” (BBC 2018), although the proposed open release of GM mosquitoes he is discussing is a small-scale release of a different technology, which the researchers expect to have no impact on malaria at all (ACB et al. 2018). A report published by the New Partnership for Africa’s Development (NEPAD) of the African Union expresses near certainty about future benefits when it states “It will certainly take many years before actual outcomes are ready for field deployment, but potential benefits for African countries against malaria will almost certainly be extensive” (NEPAD 2018, 2). Even though they may include caveats about the technology, press articles include headlines such as “Here’s the plan to end Malaria...” (Molteni 2018); “A swarm of mutant mosquitoes is out to eradicate malaria” (O’Mahoney 2018); and “A genetically modified organism could end malaria and save millions of lives — if we decide to use it” (Matthews 2018).

Target Malaria’s proposal to release up to 10,000 GM mosquitoes over the coming year is a training exercise for the researchers; Target Malaria says that these GM mosquitoes will not be used for malaria control. This is because repeated large releases would be needed to suppress the wild population of mosquitoes, which, even if successful, would be prohibitively expensive (Hayes et al. 2015, 7). Thus, there is no justification for making these releases in terms of “anticipated benefit” to public health. It is clear that the only benefit is to the researchers themselves.

A news report on the proposal to release GM mice on Nantucket describes the idea of genetically engineering mice that are immune to tick-borne diseases, such as Lyme disease, called “Mice against Ticks”, and states: “the hope is to flood Nantucket with enough of these genetically engineered mice, that they would pass the immunity gene down to their offspring for multiple generations” (Boston 25 News 2017). However, the article also states that the researchers have only “identified the genes necessary” and does not mention if they actually have any evidence that the plan would work. A year later, another article asks “Will Nantucket vote to allow genetically altered mice to control Lyme disease?” (Mullin 2018). This could be taken to imply that mice containing traits that can control Lyme disease actually exist, and also suggests that their future ability to control disease is not in any doubt.

The GBIRd website asks: “Could we create a self-limiting gene-drive modified mouse that biases future generations to be male (or female) only, thereby achieving eradication by attrition? If so, should we do it? Under what conditions?” (GBIRd n.d.). Whilst GBIRd appears somewhat more cautious about making claims of benefit than the other projects discussed here, it nevertheless implies that once the technical challenges are overcome (the creation of the genetically engineered mice) this will inevitably lead to eradication of the population. Elsewhere on the same website a similar implication is made by stating “Researchers are exploring a technique of editing rodent genes in order to produce either all-male or all-female offspring, which, once released onto an island, would effectively self-eliminate the rodent population” (GBIRd 2018). Basic practicalities, such as how many GM mice would need to be released (perhaps many times the existing mouse population, in order to successfully mate with all the mice already there) and the damage the released GM mice would do on the island during the releases, are not discussed at all.

To date, public engagement exercises by Oxitec, Target Malaria and GBIRd have been led by these companies and research programmes, all of which have vested interests in promoting high expectations of future benefits and downplaying any risks. It is hard to see such engagement exercises as independent or unbiased. For credible public engagement to take place, uncertainty about what can be delivered needs to be openly acknowledged and unrealistic promises should be avoided. These issues are discussed further in Section 10.
5.5 Summary of findings regarding claims of benefits

Promises about the future benefits of new biotechnologies are often unrealistic, due to the unacknowledged complexity of real world biological, ecological and social systems. As Chapter 4, page 219 (Ethics and Governance) of this Report notes: “these desirable consequences and benefits in welfare only obtain if 1.) gene drives can be made dependably operational, 2.) they do not come with accompanying or hidden costs to human or environmental health, and 3.) they offer a real, long-term solution”. In the case of GM mosquitoes without gene drive mechanisms it has been shown that claims of benefit, based on laboratory results and computer modelling, were not delivered in the field. In the case of gene drives, R&D is still in its infancy and far from any field trials. Many claims about future benefits of gene drives portrayed in media, scientific publications and patent applications seem farfetched. Public discussion is often limited to speculative health and conservation applications, with the aim of focusing on claimed benefits more likely to attract public support.

Framing public engagement exercises in a way that implies tremendous benefits are likely (or even inevitable), if and when open releases of gene drive organisms take place, is clearly problematic. For example, it limits the space for discussion of the usually poor success rates of so many biotechnological innovations thus far (Wallace 2010), the complexity of the approach and its dependence on numerous unverified assumptions. It also does not address the issue of the opportunity costs associated in investing in any approach that might not deliver the claimed outcomes. Further, over-hyped claims of future benefits may prevent concerns about negative impacts on human health from being included in the framing of the discussion. That is because, by definition, the still theoretical success of the gene drive organism in achieving its aim of disease reduction is assumed. It also prevents concerns about other impacts from being taken seriously because harm to ecosystems may be seen as less important than saving human lives.

Looking at biotechnology in medicine, Martin and Morrison (2006, 16) argue that in order for effective public policy to be developed, two things need to change: first, a more realistic set of expectations about the speed and scale of innovation needs to be adopted; and secondly, a different model, which views biomedical innovation as a slow and incremental process, should be used to inform public discussion and policy-making.

Similarly, McKelvey and Bohlin point out that decision-making in R&D has to be made under conditions of uncertainty about ‘what will work’ as well as about ‘what will raise capital and what will sell’. If uncertainty is widespread, then the best course of action may be to invest in a set of diverse possible directions of technological development. They note, “Certainly, biotechnology as an area of concern for basic science, small entrepreneurial firms and huge pharmaceutical companies has been one which holds out enormous promise - yet has also absorbed large amounts of resources with apparently few results in terms of direct industrial development” (McKelvey and Bohlin 2005, 98).

There is a danger that investors, policy makers and the public are being misled by unrealistic promises about what will be delivered through gene drive research and development. There may be significant opportunity costs if investments are diverted from more effective existing tools and R&D trajectories by these unrealistic promises.
6 The role of patents

As discussed above, promises about future benefits are an important means of securing research funding. Promises of potential future applications of new technological inventions or concepts are often voiced in intellectual property claims, the most stringent of which is the patent.

A patent gives its holder the right to exclude others from the reproduction, use, sale and distribution of his or her invention for a limited amount of time, generally 20 years (World Intellectual Property Organization [WIPO] n.d.). Requirements for patentability usually are: novelty, inventive step (‘non-obviousness’ in US patent law) and industrial applicability (‘usefulness’ in US patent law) (Art 52(1) European Patent Convention 2019, 27; 35 U.S. Code §§ 101-103, 2017).

The patent system is an artificial legal construct, established as a means of compensating inventors for their investments in R&D. The idea was that offering the possibility of gaining a reward would act as an incentive to create inventions and thereby foster innovation, economic growth and ultimately benefits to society. Today, however, the role of patents is controversial (see below).

In the next section, we give an overview of patents on gene drives and related technologies. We discuss what these patents cover, who the patents belong to and who they have been licensed to. Finally, we discuss whether patenting gene drive technology could be a means of regulating their use, as well as how patents on gene drives may influence innovation, research priorities and social benefits.

6.1 CRISPR-based patents

In 2014, Esvelt et al. were first to suggest using CRISPR/Cas9, a so-called genome editing technique, to build gene drive systems. This greatly boosted gene drive R&D as previous chapters of this Report have demonstrated. The CRISPR/Cas9 technology, which had been hailed as the “biggest biotech discovery of the century” (Regalado 2014), had started a flood of patent applications4. According to IPStudies, an IP consulting firm based in Switzerland, more than 2230 families of CRISPR-based patent applications had been filed by January 2018, 60% of which were filed by institutional applicants. The rest were filed by industrial applicants, individual inventors or were co-filings between industrial and institutional applicants (IPStudies 2018). The number of CRISPR-based patent applications increases monthly, with an average of 3 new patent publications per day.

The foundational CRISPR patents (Charpentier et al. 2013 and Zhang et al. 2014) have started a huge patent war between the institutional applicants and their researchers, Jennifer Doudna of the University of California, Berkeley and Emmanuelle Charpentier, then of Umeå University, Sweden, on the one hand, and Feng Zhang of the Broad Institute (affiliated with the Massachusetts Institute of Technology and Harvard University) on the other hand (see Box 1).

Box 1: War over CRISPR patents in the U.S.: UC Berkeley vs. Broad Institute

In 2012, Jennifer Doudna, University of California Berkeley and Emmanuelle Charpentier, then of Umeå University, Sweden, showed that CRISPR/Cas9, which is used by prokaryotes (bacteria and archae) as defence mechanisms against viral infections, can be reprogrammed to cut isolated DNA at a chosen site. On May 25, 2012, they filed a patent application for their invention in the US. A couple of months later, in December 2012, Feng Zhang of the Broad Institute and the Massachusetts Institute of Technology (MIT) in Cambridge also filed a patent application for the CRISPR/Cas9 technique in the US. Zhang’s team reported that CRISPR/Cas9 also works in more

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4 As of January 2019, the average pendency time (the time between filing of a patent application and the grant of the patent or abandonnement of the application, respectively) was approximately two years in the US. For individual patent applications, the pendency time might be much longer, especially if an application is being appealed and needs a decision by the Board of Patent Appeals and Interferences (BPAI) (United States Patent and Trademark Office n.d.). With a pending patent application, the applicant can, however already begin to exploit their invention (Erickson Law Group n.d.).
complex living eukaryotic cells, including plant, mice and human cells that do not have an endogenous CRISPR system. Although filed later, Zhang’s patent was granted in 2014, while the Doudna-Charpentier patent application remained under review. This led the UC Berkeley group to request an interference procedure with the US Patent and Trademark Office (USPTO). This procedure, unique to US patent law, is a means of examining whether the claims of two patents overlap and, if this is the case, who was the first to invent a commonly claimed invention. During the interference procedure, which started in January 2016, both parties filed hundreds of pages of documents with the court. The procedure moved beyond scientific argumentation and became unusually hostile, with allegations of impropriety and accusations of bias. The UC Berkeley team argued that Zhang’s application to eukaryotic cells was obvious to a “person of ordinary skills” and hence lacks ‘non-obviousness’, a condition for a patentable invention. (Ledford 2016a, b, c; Reardon, 2016; Sherkow 2017a)

The hearing, which received a lot of international attention, took place on 6 December 2016 at the USPTO. In February 2017, the US Patent Trial and Appeal Board (PTAB) ruled that there was no interference between the two inventions, which means that the Broad Institute will be able to keep its US patents. This ruling, which would give the Broad Institute control over the potentially most lucrative applications of CRISPR/Cas9 in plants, animals and humans, led to a rapid increase in the stock price of Editas Medicines, which has an exclusive licence from the Broad Institute to develop treatments for rare diseases using CRISPR, while the stock prices of its direct competitors Intellia Therapeutics and CRISPR Therapeutics, which have exclusive licences to use UC Berkeley’s patent application, fell by 10 and 15 percent, respectively (Regalado 2017; Ledford 2017).

UC Berkeley subsequently filed an appeal to the US Court of Appeals for the Federal Circuit, claiming “fundamental errors of law”; but on 10 September 2018 the US Court of Appeals upheld the previous decision by the USPTO. UC Berkeley could now still decide to appeal the decision to the US Supreme Court (Ledford 2018).

Although some were surprised about the hostile turn this patent fight has taken, a settlement was not to be expected, due to the huge commercial interests involved on both sides. The institutions behind the patents had already entered into a series of exclusive licence agreements with commercial companies founded by the institutions and one of their respective researchers. Zhang and Doudna founded Editas Medicine. Doudna, who has since cut ties with Editas Medicine, is involved with Caribou Bioscience and Intellia Therapeutics, while Charpentier has co-founded CRISPR Therapeutics with Rodger Novak and Shaun Foy (Ledford 2016a). These spinout companies had already further licensed the respective patents to other companies, including Bayer-Monsanto, DowDuPont and Novartis (Contreras and Sherkow 2017, 699) and invested millions of US Dollars in the patent fight. This system of surrogate licensing (see Box 2) of course may not be in the public interest. Editas Medicine, Intellia Therapeutics and CRISPR Therapeutics are publicly traded companies. Their duty is to maximise the profits of their shareholders and not to advance scientific knowledge in the public interest. Moreover, patent fights, where university turns against university, can complicate interinstitutional research agreements and impair the culture of scientific collaboration (Sherkow 2017b).

Box 2 University Intellectual Property Transfer

The 1980 adoption of the Bayh-Dole Act in the US allowed universities to own and commercialise patents arising from in-house inventions. Many other countries followed suit. This shift in policy reflected the growing acceptance of patenting academic research, along with the idea that social benefit could be created by licensing university patents to private firms, which would then develop commercially valuable products and services. It is now common for universities to seek to commercialise intellectual property by transferring their patent rights to private companies (sometimes co-founded by the inventors themselves), which then take on the role of further sublicensing and commercialising the invention. Contreras and Sherkow (2017) call these companies “surrogates for the institutions”. They take on the role and responsibility of the patent owner, keeping a major share of the profits. The universities, often having a substantial equity interest in the surrogate company, still receive a substantial share of the profits, while minimising their risk. In 1988, Oxford University, for example, formed Isis Innovation (now called Oxford University Innovation), a wholly-owned subsidiary designed to help the universi-
Chapter 3: Social issues

6.2 Gene Drive patents

In 2003, the first patent application describing a gene drive was published internationally (Burt 2003) The difference between national and international patent applications is described in Box 3. Therein, a method is described that has the intention of transforming a population or entire species, either for population suppression or for establishing a desired characteristic in that population. This is to be achieved by introducing a sequence-specific drive element, such as a gene with an increased inheritance ratio, e.g. a homing endonuclease gene (HEG), into the germline of an organism, thereby disrupting or knocking out a selected gene and subsequently introducing the then modified organism into the whole target population.

Long before the invention of CRISPR/Cas9 for genome editing, this patent application already described the idea of a two-component system to cut DNA at a specific target sequence and introduce the HEG at the cleavage site.

It also already described the various potential applications of gene drives, still being promised today: malaria control (either by mosquito population control or by conferring resistance to the malarial parasite); eradication or control of unwanted or colonising species which are detrimental to a previously-established ecosystem (for example rodents or goats); altering the balance of insects or microorganisms (for example those associated with food crops or livestock); or rendering pests susceptible to appropriate pesticides (for example insects, nematodes or fungi).

Its inventor, Professor Austin Burt, is now a member of the ‘Gene Drives for Vector Control’ group at Imperial College, which is one of the partner institutions of Target Malaria, and is Target Malaria’s Principal Investigator. As well as patents on CRISPR technology or gene drives, academic institutions may also hold related patents on particular applications. Other members of the ‘Gene Drives...
for Vector Control’ group at Imperial College, for example, have applied for patents to genetically modify insects, particularly malaria-transmitting anopheline mosquitoes (see Box 4). These are relatively old patent applications that may not apply to gene drive organisms, but they illustrate how GDOs developed in the future might also be patented, along with how academic scientists and institutions may already have (or may develop) commercial interests in particular technologies.

Box 4. Related patent applications from the ‘Gene Drive for Vector Control’ Group

In 2000, Crisanti et al. applied for a patent to genetically modify insects, particularly anopheline mosquitoes, by introducing foreign genes in the *Anopheles* genome. Therein, they provided a.) a method to delay the hardening process of the chorion, the rigid structure around the insect embryo, after oviposition so as to facilitate DNA injection; and b.) a DNA delivery vector capable of successful transposition in anopheline mosquitoes. They suggest either introducing a gene to control the transmission of malaria-causing parasites or producing sterile males intended to be released as a means of genetic control.

In 2004, Kafatos et al. applied to patent a method to render anopheline mosquitoes, in particular *Anopheles gambiae*, resistant to malaria-causing parasites. The method describes how to enhance or suppress mosquito proteins, that are either hostile or beneficial for parasite development, by application (feeding, spraying or injection) of a compound that interferes with the expression or activity of the protein. It further describes how to identify compounds that trigger an immune response in a mosquito of the genus *Anopheles* against *Plasmodium* (the parasite). For suppression of the protein expression, their suggestion is to use antisense-technology, or RNA interference (RNAi) in order to knock out the described genes.

With the discovery of the CRISPR/Cas9 technology, a dozen gene drive patent applications have followed, most of which either belong to Harvard University or the University of California (Table 1).

A key gene drive patent application, called “RNA-Guided Gene Drives” and filed by Harvard University (Esvelt and Smidler 2015), claims the ability to develop a method for targeted population suppression or extinction via the release of an RNA-guided genetic load drive into the targeted population, thus biasing the sex ratio of the population. The patent application describes the utility of this gene drive in the eradication of infectious diseases, the control of invasive species and the protection of threatened species, such as amphibians. However, the major part of the patent description is dedicated to “Agricultural Safety and Sustainability” and what they call “sensitising drives”. Sensitising drives are gene drives meant to render the progeny sensitive to an external stimulus. This means that exposure of a weed or pest to a compound, for example a specific chemical, should result in a harmful reaction. The idea is to make pesticide-resistant weeds or pests susceptible to the original pesticide again - a major commercial ‘rescue operation’ for what have been failing markets for chemicals like glyphosate, due to the pests developing resistance. Subsequently, hundreds of weeds, crop pests and pesticides became covered by the patent, including glyphosate, 2,4-D and Bt toxins produced by CryIA.105, CryLAb, CryIF, Cry2Ab, Cry3Bb1, Cry34Ab1, Cry35Ab1, mCry3A, or VIP (Esvelt and Smidler 2015, 34–51). The same weeds, crop pests and pesticides are covered in a 2017 patent application, also by Harvard University (Esvelt and Min 2017, 42–60). In these ways, using and adapting the patenting system, academic science has been further integrated into the global agrichemical and GM industries. Along with other important domains, and with little democratic attention, gene drives have also become a driver of this transnational social and political change.

This shows that gene drives may be able to attract lucrative investors in the agricultural field of genetically modified (GM) crops. The most widely commercialised GM crops engineered to be resistant to herbicides, such as glyphosate and different insecticidal toxins derived from *Bacillus thuringiensis* (Bt), have suffered major set backs with the development of glyphosate-resistant weeds and insect pests that are now resistant to Bt toxins (Bohnenblust 2016; Peralta and Palma 2017), something long predicted by those opposing this technology. Alternative GM crops, such as those resistant to the herbicides dicamba and 2,4-D, have led to huge problems with
herbicide drift when these crops are treated with their very toxic corresponding products, resulting in millions of acres of incidental crop and non-crop injuries in the US (Bohnenblust 2016; Bradley 2017; 2018). Moreover, multiple weed resistances to glyphosate, dicamba and 2,4-D are already seen today (Dellaferrera et al. 2018). Recently, hybridisation between two major agricultural pest insects (H. armigera and H. zea) has been confirmed, raising additional concerns about increased insecticide resistance problems in the future (Anderson et al. 2018).

Any technology that claims to be able to reverse these resistances is likely to attract the attention of the major biotech companies, many of which already have license agreements for using CRISPR/Cas9 (see above). In 1993, when applying for non-regula-

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<td>Method for Autocatalytic Genome Editing and Neutralizing Autocatalytic Genome Editing</td>
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<td>Methods of genetically altering yeast to produce yeast variants</td>
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tion status of the first genetically modified Roundup Ready (glyphosate tolerant) soybeans, Monsanto claimed incorrectly that it was “highly unlikely that weed resistance to glyphosate will become a problem as a result of the commercialization of glyphosate-tolerant soybeans” (Monsanto 1993, 56). With the development of yet more genetically modified crops, allowing spraying of more and higher levels of herbicides, we face a form of herbicide intensification termed ‘the transgenic treadmill’ (Binimelis, Pengue, and Monterroso 2009, 9; Schütte et al. 2017, 7). In the case of gene drives, scientists now agree that resistance could eventually evolve again, but discard the whole problem by saying this technology could be used repeatedly to make weeds and pests susceptible again and again (Champer, Buchman, and Akbari 2016, 147). It seems evident that this would lead to a new level of treadmill,

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whose purpose is not to prevent diseases or pests, but to maintain the prevalent chemically-dependent industrial agricultural system.

Another fundamental gene drive patent application, this one filed by the University of California and called “Method for Autocatalytic Genome Editing and Neutralizing Autocatalytic Genome Editing”, mentions applications for combatting malaria, HIV and cancer and in reducing or eliminating immunogenicity, as well as in controlling agricultural pests and invasive species (Bier and Gantz 2016). It further includes hundreds of cancer types and model organisms, many of which are agricultural pests, thereby also covering potential lucrative applications in the health and agricultural sectors.

In 2017, MIT and Harvard University applied for a patent on daisy chain gene drives, a type of gene drive that is not yet functional, but would be “…designed to permit controlled, local gene drive activity.” and claims to have “the ability to confine the gene drive organisms, such that they only affect local populations and do not risk global gene drive activities” (Esvelt, Min, and Noble 2017, 33). According to the patent, daisy chain gene drives may be used to reduce vector-borne and parasitic diseases, as well as to control or eliminate populations of agricultural pests or invasive species. Non-limiting examples of organisms which a daisy chain gene drive may be delivered to, or included in, according to the patent, are: “insects, fish, reptiles, amphibians, mammals, birds, protozoa, annelids, mollusks, echinoderms, flatworms, coelenterates, and arthropods, including arachnids, crustaceans, insects, and myriapods” In 2018, MIT and Harvard University applied for another patent on daisy chain gene drives, covering the same non-limiting examples of organisms (Esvelt, Min, and Noble 2017, 52; Esvelt, Min, and Noble 2018, 48). This kind of comprehensive patent ownership is not uncommon in patenting of genetic research. The fact is that most of the domains listed have never been tested even in a preliminary way for the effectiveness of the gene-drive; they have simply been imagined by the researchers as possible domains. This illustrates how institutions and academic researchers try to foresee and legally cover any potential future commercial exploitation of their invention.

The idea of using locally confined gene drives might seem more responsible, reducing ethical concerns about potentially eradicating entire species along with safety concerns about unintended and unforeseeable consequences. It means the prospect of developing daisy chain gene drives could increase public support for the technology. Along with funding, public understanding plays an important role when it comes to governance and regulation of new technologies (Mitchell et al. 2018, 3), so the development of “local gene drives” would also likely attract more private investment. A technology that potentially spreads to an entire population or species after an initial release is not as likely to develop a huge commercial market, hence the return on investment might be limited. With the possibility of spatially and temporally confining the spread of a gene drive organism, however, multiple subsequent releases at multiple locations are imaginable (Mitchell et al. 2018, 4). Going back to the theory of “sensitising drives”, as explained above, a private company might be able to sell a package of a compound (such as a pesticide) and a corresponding gene drive organism (such as a crop pest) that has been rendered sensitive to said compound, each and every year to farmers around the world. These kinds of strategic and competitive business models, should in principle require democratic appraisal, since they have far-reaching and often unpredictable social, environmental, and economic consequences.

6.2.1 Regulation of Gene Drive patents

Esvelt has suggested that the patent system could be used to ensure gene drives are used ethically and responsibly. Those wanting to purchase a patent license would first have to disclose their proposed use to the patent holder before carrying out any experiments. The goal would be to ensure openness and also to limit licenses only to users ensuring ethical use (Regalado 2016c; Sherkow 2017b). Although this seems like a noble suggestion, this would mean that Esvelt himself and Harvard University, or any other scientist and their employ-
er-institution which had been granted a gene drive related patent, would be able to decide how gene drives should be used or what constitutes an ethically justifiable purpose. In so doing, they would take on the role of gene drive regulators, gaining legal control over not just the technology disclosed in their patent, but its distribution and use.

This would inevitably fragment the larger social regulation of the entire technology. A societal responsibility like gene drives (or any other technology) governance should not be placed in the hands of a research institution or individuals, most especially those who have a direct financial interest in its promotion. Those with vested interests in the technology cannot also be the ones overseeing its governance and use. How could it be ensured that the foundational gene drive patents, covering many potentially lucrative applications in the health and agricultural sector (see above), are not licensed to a few surrogates that are really part of larger companies, as has happened to the related CRISPR/Cas9 patents? In the end, society would have to put its trust in the patent holders alone to ensure that the technology is used (or not used) in the best public interest.

Instead, Parthasarathy (2018, 488) argues that transparency and political legitimacy would increase if government institutions, which are explicitly charged to represent the public interest, were to use patent systems to help regulate new technologies such as gene editing. The patent system would have to be linked to explicitly relevant laws for the purpose of regulation. In the US, this was already done in the Atomic Energy Act of 1946/1954, to reduce the development and commercialisation of atomic weaponry by private actors. This Act, for example, prohibits the patenting of any invention or discovery that would be “useful solely in the production of fissionable material or in the utilization of fissionable material or atomic energy for a military weapon” (Newman and Miller 1947, 750). If a patent for a production device could be obtained, the inventor would not be allowed to manufacture the device without a license from the Atomic Energy Commission, nor could they license its use to anyone except the government. If an intergovernmental regulatory framework for reviewing and awarding patents for their ethical and responsible use was set up, the patent system might indeed add another layer of protection from misuse of the technology. It cannot, however, be left to the patent system alone to regulate gene drives.

6.3 Social benefit implications of patents

The intent of the patent system is to increase innovation and enable the development of commercially valuable products and services, in order to create economic growth and ultimately social benefits. However, today the role patents play in fostering social benefits is ambiguous. As noted by the OECD, research and innovation thrive on collaboration and knowledge sharing (Gold et al. 2008, 16). Patent holders are required to publicly disclose the details of their inventions so that others can build on it by undertaking further research and development. At the same time, a patent, by definition, is the right to exclude others from commercially using the given invention. It has often been claimed that industry manipulates patent law to thwart rivals and block research, as well as to direct it away from humanitarian goals towards goals that maximise profits (Jenkins and Henderson 2008). In the health field, for example, despite increasing use of intellectual property patents, a decline in innovation has been observed (Gold et al. 2008, 7). As the example of CRISPR/Cas9 has shown, the commercial interests behind patents on biotechnological inventions often foster secrecy and hamper transparency and collaboration, thus interfering with overall innovation dynamics.

Kevin Esvelt, who openly opposes closed-door science, agrees that the current competitive approach to scientific enterprise doesn’t promote open and transparent science: “It is a prisoner’s dilemma. The benefits come from cooperation by everyone. But by participating you risk being exploited by people who steal your idea, get it working before you do, and claim the credit.” (Esvelt 2016, 153). Gene drive research, however, would, according to Esvelt, offer a way out: “The field is new and small, and many of us have already worked together to publish a joint
recommendation calling for future experiments to use multiple stringent confinement strategies. Several groups already disclose proposed and ongoing gene-drive research and invite feedback, and active discussions between researchers and funders seek ways to ensure that everyone will be similarly forthcoming.” (Esvelt 2016, 153). In 2016 he and his colleagues initiated the project “Responsive Science”, intended to further this vision.

While the efforts of Esvelt and colleagues, to disclose their research ideas and foster open discussion (even before the experiments are performed), is very laudable, it is unfortunately questionable whether all gene drive researchers will follow Esvelt’s call, as all he is doing is appealing to the individual scientists’ sense of responsibility. He suggests no means of enforcing participation or controlling whether or not the rules he discusses are being followed. Furthermore; (1.) the appropriate rules would need lengthy negotiation amongst relevant parties; and (2.) those relevant parties would have to include institutions as well as individual scientists, and it is well-attested that institutions behave in ways which cannot be modelled from individual behaviour.

Patent rivalry between universities is not the only reason that scientists don’t want to disclose their research ideas. Disclosing an idea to the public at an early stage may itself affect later patentability of related innovations. This in turn may decrease the likelihood of finding the funding that can translate the idea into reality (Fass et al. 2011, 11). Esvelt suggests that gene drives should be a non-profit technology (Esvelt 2018b), even if it would mean repercussions for his personal benefits from his patents. The same, however, cannot be expected from others, and it is questionable if everyone involved in gene drive R&D would agree (and could afford) gene drives to be a non-profit venture. Moreover, it has to be noted that the motive behind Esvelt’s suggestion is unlikely to be free access to the technology (see Section 6.2.1, Regulation of gene drive patents) but rather public acceptance and the avoidance of a moratorium on gene drives. In a 2018 article titled “Gene drive should be a non-profit technology” Esvelt states: “When people know you will benefit financially from a proposal, they’re less likely to trust your judgment”, adding: “Gene drive and other ecotechnologies depend on popular support. Since they involve the genetic engineering of wild populations, that support is by no means guaranteed, especially if there is for-profit involvement.” (Esvelt 2018b). However sincere his personal beliefs might be in terms of this technology bringing social benefits, such statements leave the impression that Esvelt’s engagement for openness and transparency in science is as much a strategic choice to gain public acceptance, in order to move forward quickly, as it is a willingness to foster true public engagement. A lack of the latter in practice could delay or even lead to the rejection of the technology: “The primary danger posed by CRISPR-based gene drive is social. Given widespread scepticism of genetic engineering, any unauthorized release of a gene drive system could lead to a strong social backlash and serious damage to public trust in science and governance when society can least afford it. In addition to institutional damage, such backlash would almost certainly delay efforts to use gene drive to prevent vector-borne and parasitic diseases such as malaria and schistosomiasis, possibly resulting in millions of otherwise preventable deaths.” (Esvelt 2018a). Furthermore, the issues described in this chapter also apply to non-profit enterprises, which have their own in-built social biases and assumptions, and which may also wield significant power over others.

Another important social issue highlighted by the increased use of patented technologies, one which has been less widely discussed, is the effect that patents have on research priorities. The role of patents is not straightforward and is often difficult to disentangle from the other factors influencing R&D investments and innovation. However, possible negative impacts of university patenting include diverting research resources (researchers’ time and equipment) away from research questions that may not to be suited to the development of patents, but which may well offer potentially greater social benefits (Geuna and Nesta 2006, 799). As numbers of patent applications and income from intellectual property have become measures of university and industry success and funding, patentable inventions
will be given a higher priority over other types of research that might have greater social benefit. It is thus not only access to biological knowledge and discoveries that is controlled and shaped by the patent system, but also what constitutes scientific knowledge itself (Wallace and Mayer 2007).

With the rise of biotechnology, patents were legalised for living organisms for the first time in 1980 in the US (see Diamond v. Chakrabarty), and globalised in the 1995 Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement. The possibility of patenting genetically modified organisms in turn was a major incentive to further invest in genetic engineering, as it allowed patent owners to control and exploit genetic material that farmers previously freely replanted and exchanged amongst themselves. Although it is clearly not the only factor driving research agendas, the commodification of genetic inventions via patent claims therefore plays a key role in the ‘geneticisation’ of both health and agriculture.

As mentioned, gene drive R&D is accompanied by promises of many beneficial applications. However, open releases of gene drive organisms have the potential of altering and interacting with ecosystems in new, complex, unpredictable and unforeseeable ways. Whether or not the deployment of gene drive organisms will in fact create social benefit one day is still very hypothetical. Nevertheless, gene drive technology hype and patents may help attract further investment in gene drive R&D and possibly divert resources from potentially more sustainable alternatives.

7 Fully informed consent

In this section, we consider issues related to the need for individuals to provide prior, fully informed consent to open releases of GDOs.

7.1 Fully informed consent for projects not involving medical research

For medical research such as releases of gene drive mosquitoes, fully informed consent is already an ethical requirement under the Helsinki Declaration (see Section 7.2). However, for other gene drive organisms, which are intended to alter ecosystems but not to impact on human health, the situation so far has been less clear. This changed in 2018 with the adoption of a decision by Parties to the Convention on Biological Diversity (CBD), as discussed in Chapter 5. This requires the consent of potentially affected indigenous peoples and local communities to be sought or obtained to the release of GDOs “where applicable in accordance with national circumstances and legislation”. The CBD Decision is an important acknowledgement of the importance of consent to the release of any GDO; however, for medical experiments, any release will also have to comply with the more stringent and well-established requirements of the Helsinki Declaration, as discussed below.

7.2 Fully informed consent to medical research

In the case of releases of gene drive mosquitoes with the goal of affecting tropical diseases such as dengue fever or malaria, the requirement for fully informed consent is enshrined in international principles for medical research.

The Declaration of Helsinki outlines the internationally agreed ethical principles for medical research involving human subjects (World Medical

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5 The subsequent rise of a few agrochemical companies that today control a major share of the global seed and pesticide markets, and its impact on farmers’ and consumers’ choice, is still subject of controversy today. Others critique the patenting of life altogether (see for example the German and European initiatives “Kein Patent auf Leben!” and “NO PATENTS ON SEEDS!”, respectively).
Association 2013). It includes the requirement that: “Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects” (Article 16).

The Declaration of Helsinki builds on the Nuremberg Code, adopted as a code of medical ethics to condemn the practices of doctors working for the Nazis (Fischer 2006). It also states that: “In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study...” (Article 26).

Thus, the Helsinki Declaration requires that research participants are adequately informed about the risks and anticipated benefits of the study. In theory, this allows potential participants to weigh up the potential risks and benefits, as part of the process of informed consent.

Resnik (2012) explores a hypothetical field trial of malaria-resistant GM Anopheles mosquitoes and highlights the fact that field trials should not be implemented unless research indicates that overall public health benefits are likely to be greater than public health risks (Resnik 2012, 5). He further notes that, “In a study taking place in a developing nation, it is likely that many of the subjects will be vulnerable, due to poverty and lack of access to health care” and notes that, “To protect these subjects, measures should be in place to ensure that consent is free from coercion and undue influence” (Resnik 2012, 7). Resnik also states that, “Individuals may be exploited if they are harmed in research when there is little expectation that they will benefit, or they do not provide consent” and that, “Exploitation of a community may occur when the community is placed at risk without the expectation of significant benefits” (Resnik 2012, 7).

Macer (2005) also considers ethical issues in relation to the release of genetically modified (GM) insects with the aim of controlling human disease. He notes that “Informed consent requires information to be provided, so disseminating information about the plans and progress of the project, and obtaining the consent of any person potentially affected by the release of transgenic insects, is important for the ethical conduct of research trials, whether or not national guidelines require this, or even exist” (Macer 2005, 653). Macer also highlights that if a study involves humans, oversight by an ethics committee or institutional review board (IRB) is also necessary (Macer 2005). He goes on to argue, “To consider the issue at a local level, as required for obtaining appropriate informed consent, it is essential that a local ethics committee (and/or IRB if associated with an institution) open to the communities involved is established” (Macer 2005, 654).

This raises issues about how these risks and benefits are determined and communicated, and how different value-judgements, unknowns and uncertainties are dealt with in this process. Aspects of these issues are covered by national and international agreements and regulations covering genetically modified organisms (GMOs). However, these regulations may be absent, contested, or not properly enforced. Below, we consider how risks have been dealt with to date during the process of obtaining consent for projects wishing to release GM mosquitoes (currently without gene drive). We highlight that in practice participants may not be fully informed by developers about the risks of new technologies and that power asymmetries may affect who has information, what choices people are able to make, and whose voices are heard. Hype about benefits will also substantially affect whether people are genuinely fully informed before they are asked for their consent.

### 7.3 Absence of adequate environmental risk assessments

The previous section highlighted the problems associated with the ethical requirement upon scientists to obtain fully informed consent from all potentially affected parties before they begin any environmental releases. For “fully informed” to be
a meaningful condition for the public, scientists involved also have to be fully informed about all possible harms that may result from their actions. This is a problematic normative condition. As Chapter 4 (Ethics and Governance) notes, risk assessments inherently involve making value-based judgements; for example, deciding what constitutes a hazard or an environmental protection goal, and what constitutes quality in safety science. This involves being explicit not only about imprecisions in knowledge of salient measures and relationships ("uncertainties"), but also about lack of knowledge ("ignorance"), and untested assumptions ("ignorance"), as well as about unanticipated contingencies (also ignorance, e.g. variable conditions in the environment which may affect validity of assumed extrapolations to broader conditions). Risk management decision-making also inevitably requires a determination of what constitutes an acceptable level of risk.

Both Oxitec’s and Target Malaria’s GM mosquitoes have been exported from European Union (EU) countries for open release into the environment elsewhere. Under EU law, the exporter should provide prior notification, including a publicly available environmental risk assessment that meets European standards, before exporting GM insect eggs for open release to foreign countries. This legal requirement arises because GM insect eggs are live, genetically modified organisms (living modified organisms or LMOs) covered by the Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity. The relevant legal requirements for export are implemented in the EU through the European Regulation (EC) 1946/2003 on transboundary movement of genetically modified organisms. This Regulation requires that the environmental risk assessment (ERA) provided by the exporter meets the EU standards on risk assessment contained in EU Directive 2001/18/EC. Regulation (EC) 1946/2003 is important because it requires the exporter to provide a comprehensive, publicly available risk assessment that meets EU standards for GMOs intended for release into the environment. The Precautionary Principle (discussed in Section 8) must be taken into account when applying this Regulation.

Avoidance of transboundary notifications has been a major issue with the commercial GM insect company Oxitec, which has never published a risk assessment which meets EU standards prior to undertaking any of its open releases of GM mosquitoes into the environment (GeneWatch UK 2014). Reeves et al. note that there were “significant omissions” (Reeves et al. 2012, 8) in the information made publically available prior to open releases of GM mosquitoes in the Cayman Islands and Malaysia, and that “Without the pre-release publication of complete risk assessment documents detailing all the potential hazards analyzed, it is often impossible to establish which have been considered (and by whom) and if any obvious hazards have been overlooked for rigorous consideration” (Reeves et al. 2012, 9). They also highlight that the Cayman Islands had no enacted legislation relating to living GM organisms at the time of the first open release of GM mosquitoes there (Reeves et al. 2012, 8).

Target Malaria has claimed to be holding itself to higher standards. However, it is currently arguing that it is not required to make a transboundary notification that includes such a risk assessment for its proposed release of male-sterile GM mosquitoes in Burkina Faso, because the GM mosquitoes were exported for an initial period of contained use (for which a notification is not required under EU law) before release (ACB et al. 2018). Instead, Target Malaria has commissioned its own risk assessment, without reference to the required standards, which omits some of the relevant issues, and relies heavily on ‘expert elicitation’ and unpublished data (Hayes et al. 2018).

In September 2018, Target Malaria announced that it had received regulatory approval for its first proposed open release of GM mosquitoes in Burkina Faso (Target Malaria 2018). However, there is no published environmental risk assessment (ERA) other than one published by Target Malaria itself, and there has been no public consultation, apart from “public engagement” activities conducted by Target Malaria, the organisation proposing the release. This is despite the fact that the Cartagena Protocol requires Parties, including Burkina Faso, to make available summaries of the risk assessments
generated by its regulatory process to the Biosafety Clearing House (paragraph 3(c) of Article 20), as well as to consult the public in the decision-making process (paragraph 2 of Article 23) (see also Chapter 5, Regulation).

According to the Helsinki Declaration, people must be fully informed about the potential risks of a study in order for their consent to meet ethical requirements. This cannot be the case until a comprehensive risk assessment has been published that meets the necessary standards and opened for public consultation. Because the idea of releasing GM insects into the environment is relatively new, best practice would be for specific guidance on how to do such risk assessments first be developed by the regulators, not the proponents, and for this guidance to be subject to public consultation, such as has happened in the EU (EFSA Panel on Genetically Modified Organisms 2013). Provided conflicts of interest can be avoided, this could help prevent the developer having too much influence over the risk assessment process, including how unknowns and uncertainties will be handled.

In addition, under the Cartagena Protocol, Parties are allowed to take into account socio-economic considerations that arise from the impact of GMOs on biological diversity when they make decisions about importing GMOs. Under national laws, socio-economic considerations or assessments may also be required as part of decision making on GMO applications.

ERAs published to date for GM insects have not included any discussion of socio-economic aspects. The summary of the risk assessment commissioned for Target Malaria’s proposed release of GM mosquitoes on Burkina Faso states, “The report is not a complete evaluation of all potential risks. Some potential risks, such as the risks to social endpoints identified in Burkina Faso’s legislation, are not addressed in this analysis” (Hayes et al. 2018, 2). This sidesteps the question of where these missing social risks have been evaluated or how the public will be informed about any such assessment, as well as if they will be engaged in any decision-making (see Section 10). This issue will remain relevant for future proposed releases of GDOs (whether proposed by Target Malaria or others).

It should be noted that open releases of GDOs would challenge the regulatory system further, requiring updates and adaptations to GMO risk assessment methodologies as well as a precautionary approach (discussed in Section 8).

7.4 Power asymmetries

As noted above, power asymmetries may be particularly evident when technologies are transferred from wealthy to poor countries, and when the people affected may be vulnerable, not only because of their poverty, but because the state and related infrastructures are typically much weaker in poor countries.

In African countries, there have been a few studies of public and scientific attitudes to the release of GM mosquitoes which would potentially include gene drives. Preliminary research conducted in Burkina Faso concluded that “the community’s acceptance of GMM [GM mosquito] release could be affected by the fact the citizens interviewed did not appear to completely understand either the possible negative aspects of GMMs in the environment or the detail of how GMMs operate” (De Freece et al. 2014, 265). In a small study of perspectives of people in Mali toward GM mosquitoes for malaria control, 62 participants said they would support a release of GM mosquitoes that satisfied their conditions, 14 said they would not support a release under any circumstances, and four were unsure (Marshall et al. 2010, 7). Conditions were wide-ranging and included requirements for evidence GM mosquitoes will not cause human health or environmental concerns and that there would be no costs to the community (Marshall et al. 2010). However, it is not at all clear how these conditions might be implemented and enforced.

Notably, Marshall et al. reports that, “The main concern expressed by participants in all groups, but particularly amongst those from rural areas, was that the strategy of releasing GM mosquitoes will not
work” (Marshall et al. 2010, 7). This is an important issue in view of the general over-optimism concerning the technology discussed above, as well as the untested claims of efficacy that are often made by GDO developers. To what extent can claims of efficacy (as well as risks) be contested in debate about new technologies? How can potential participants, who may lack resources and technical expertise, raise concerns about efficacy that are not dismissed by the scientists who have a vested interest (financial, or otherwise) in promoting such technologies? Finally, can people have any influence on research investments and the exploration or implementation of alternatives? These issues are discussed further in Section 10.

In some cases, power imbalances may occur not only between ‘experts’ and local people, but also between the relatively well-funded scientists promoting an open release of GDOs and local scientists or medical experts. Okorie et al. (2014) interviewed 164 scientists selected from academic and research institutions in Nigeria and found that a majority (83.5%) of the local scientists who participated in their study were sceptical about a potential release of GM mosquitoes in Nigeria. Further, 92.7% of these scientists would require contingency measures to be available to remove the GM mosquitoes “should a hazard become evident during the course of the release” (Okorie et al. 2014, 1).

Looking beyond debate about the benefits and risks of the experiment itself, Marshall et al. noted that some of their interviewees in Mali seemed to accept the proposed GM mosquito project for reasons unrelated to their actual feelings about the technology, in this instance “based on the expectation that they will get a hospital in return” (Marshall et al. 2010, 11). They also noted the limited participation of women in their study.

In the case of Target Malaria, concern about the process of informed consent is exacerbated by evidence that the company is paying 400 CFA francs (approx. 70 cents US) per hour to people collecting biting female mosquitoes from their own bodies (Flanagan 2018). Volunteers are required to sit for 6 hours in a room at night with the lower part of their leg exposed up to the knee, so that the mosquitoes land and they can collect them with a suction tube (Target Malaria Burkina Faso and IRSS 2017). The use of a financial incentive to induce individuals to expose themselves to biting female mosquitoes, that is, potentially to contracting malaria, is ethically very questionable, and highlights a power imbalance between the researchers and research participants underpinned by great financial inequalities.

An independent report from Burkina Faso has detailed further concerns. It found that many people in the country are concerned about the potential impacts of Target Malaria’s project and about the absence of risk assessment by the regulators, and are unaware of many of the details of the project, including where the funding for the project comes from (Fuhr 2018).

Target Malaria’s lead funder, the Gates Foundation, is one of the largest on earth and extremely influential. Whilst its generosity has been widely praised (it spends more on global health every year than most countries), it has also been criticised for unknown efficacy, since the process is answerable only to the Gates family and therefore lacks accountability and transparency. This foundation has also been accused of what some regard as questionable priorities, in particular, too much emphasis on technology and technological fixes. It also supports strong intellectual property (IP) protections within these supposedly philanthropic projects. Finally, few people involved are willing to speak on the record about any concerns in these and other regards because they are being funded by the foundation (Belluz 2015). Emails released as a result of Freedom of Information requests and published as the Gene Drive Files reveal that a previously undisclosed gene drive “advocacy coalition” was run by a private PR firm, which received $1.6 million in funds from the Bill and Melinda Gates Foundation. The firm is on record at the UN for employing covert lobbying tactics to influence expert UN discussions (Gene Drive Files 2017c).

There is little public information regarding the consent process used by Target Malaria. However, NGOs and journalists have reported concerns about
other power imbalances, including from a woman highlighting her difficulties from within the community asked to give its consent, who told Le Monde “In any case, we do not have our say, it is the men who make the decisions here” (Dossou 2018; Douce 2018; Noisette 2018).

Power imbalances can also influence regulatory processes. In 2012, a group of NGOs published a report detailing how Oxitec had infiltrated decision-making processes around the world with a view to influencing regulations, guidelines and decision-making about the release of genetically modified insects (GeneWatch UK 2012). Subsequently, the European Ombudsman found that one of the experts involved in developing guidance for the risk assessment of GM insects in the EU had failed to declare relevant conflicts of interest (European Ombudsman 2015).

Thus, power imbalances may affect the regulatory framework and who is asked for their input to decisions, as well as influencing whose voices end up being heard and, ultimately, what decisions are taken.

8 Precautionary Principle

8.1 The need for a precautionary approach

A precautionary approach involves adopting a cautious attitude towards risk that takes pre-emptive measures to avoid harm (see Box 1 in Chapter 4: Ethics and Governance). It is an explicit commitment for all signatories to the UN Convention on Biological Diversity (CBD) and its Cartagena Protocol.

8.2 Brief history of the Precautionary Principle

Although the Precautionary Principle was originally anchored in the concept of prevention used in medicine, it has expanded its intrinsic notions of prevention into a general rule of public policy action and participation in matters that represent potential threats to health and the environment. According to Harremoës et al. (2001), writing on the history of the Precautionary Principle, the concept arises from the German Vorsorgeprinzip first introduced in 1974 by the German Clean Air Act. Since this date, the principle has been progressively integrated in political agendas and international agreements, expanding not just the scope and range of the principle, but also its names, which has resulted in a sometimes confusing discussion over terminology.

Wynne (2002, 469) argues that scientific risk discourse wrongly implies that risk analysis identifies all significant future consequences of the relevant actions. It thus ignores (or “deletes”) ignorance and the unanticipated consequences – lack of control – lying beyond the reach of existing scientific knowledge. Wynne (2002, 465) argues that the dominant risk discourse also excludes many other questions, which he distils into three general types: 1.) other issues and interconnections, such as driving purposes, intended social benefits, and conditions (e.g. of ownership, implementation, investment and control, regulation and accountability); 2.) what is meant by ‘the technology’ as putative ‘cause’ of possible impacts; and 3.) are the consequences or questions even answerable, and if not, what then?

Stirling highlights that, “precaution is not simply about acting to stop something, but introduces instead a responsibility for more careful and explicit reasoning over what kinds of action might be appropriate” (Stirling 2016, 5). Further, “In particular (and unlike idealised notions of ‘sound scientific’ risk assessment), it embodies an awareness of the asymmetries and inequalities of the power relation-
ships that bear on processes of regulatory appraisal and help to shape the fabrics of the knowledges produced within them” (Stirling 2016, 5). Therefore, “the Precautionary Principle requires more explicit, scientifically rigorous and socially sophisticated attention to the implications of incomplete knowledge, than is routinely provided in the conventional regulatory assessment of ‘risk’” (Stirling 2016, 6).

According to Harremoës et al. “The precautionary principle is an overarching framework of thinking that governs the use of foresight in situations characterised by uncertainty and ignorance and where there are potentially large costs to both regulatory action and inaction” (Harremoës et al. 2001, 192). Harremoës et al. describe twelve ‘late lessons’, based on an analysis of case studies, which highlight the importance of heeding ‘early warnings’ and taking a precautionary approach. Their case studies include examples of harm caused by X-rays; lead (and lead substitutes) in petrol; asbestos; poorly managed fisheries; ‘mad cow’ disease (BSE); radiation; and various chemical pollutants. The lessons drawn by the editors of the report are:

1. Acknowledge and respond to ignorance, as well as uncertainty and risk, in technology appraisal and public policymaking.

2. Provide adequate long-term environmental and health monitoring and research into early warnings.

3. Identify and work to reduce ‘blind spots’ and gaps in scientific knowledge.

4. Identify and reduce interdisciplinary obstacles to learning.

5. Ensure that real world conditions are adequately accounted for in regulatory appraisal.

6. Systematically scrutinise the claimed justifications and benefits alongside the potential risks.

7. Evaluate a range of alternative options for meeting needs alongside the option under appraisal, and promote more robust, diverse and adaptable technologies so as to minimise the costs of surprises and maximise the benefits of innovation.

8. Ensure use of ‘lay’ and local knowledge, as well as relevant specialist expertise in the appraisal.

9. Take full account of the assumptions and values of different social groups.

10. Maintain the regulatory independence of interested parties while retaining an inclusive approach to information and opinion gathering.

11. Identify and reduce institutional obstacles to learning and action.

12. Avoid ‘paralysis by analysis’ by acting to reduce potential harm when there are reasonable grounds for concern. (Harremoës et al. 2001, 168–169)

The most frequent argument coming from opponents to the application and expansion of the Precautionary Principle has been that it slows or even interrupts the innovation and development process. But as the editorial team from “Late lessons from early warnings: the precautionary principle 1896-2000” (Harremoës et al. 2001) has demonstrated, there is no empirical evidence to support such an argument. On the contrary, according to the editorial team and based on the fourteen case-studies that are the basis of their argument, the Precautionary Principle will only restrict innovation in some questionable technologies, while creating the space to foster innovation in other directions. These favoured technologies are often ones which may not be under the control of, or are otherwise not favourable towards, global industrial interests and their particular investments. This has demonstrated that curtailment of a particular option may actually serve to foster and intensify innovation, but in other areas (Harremoës et al. 2001, 182). The actual objection to applying the Precautionary Principle really seems to be that the technological pathways developed under it may not be the ones endorsed today by corporate and private interests. Stirling (2016) argues that precaution is about steering innovation,
not blocking it, as innovation can take many different pathways. He concludes “In the end, precaution is identified to be about escaping from technocratic capture under which sectoral interests use narrow risk assessment to force particular views of the world. What precaution offers to enable instead is more democratic choice under ever-present uncertainties, over the best directions to be taken by innovation in any given field” (Stirling 2016, 2).

8.3 Application of the Precautionary Principle to research

The dominant linear and reductionist approach to risk assessment is problematic, especially because of the many ambiguities, complexities and indeterminacies inherent in human knowledge. The twelve lessons above, highlighting problems which can occur due to the lack of application of a precautionary approach (Harremoes et al. 2001), have in fact demonstrated that science may be insufficiently reflexive and critical about the potential good and harm caused by its activities. The optimistic aura surrounding the promises of science and technology along with the excessive expectations that aura has fostered, has perhaps obscured the capacity to accept the fact that ignorance, uncertainty and risk are part of the scientific system. The current atmosphere accompanying any new technology (which is “hyped” in order to stimulate acceptance and funding), has created a distinction between how scientific uncertainty and change are accepted within the scientific community, compared with how they are downplayed outside it. These true descriptions of how science works tend to disappear when scientific researchers seek to provide society with unrealistic certainties in order to gain funding.

Stirling details how “various forms of the precautionary principle serve, in many specific ways, to help foster more transparent and deliberate democratic decision making concerning the steering of alternative directions for innovation” (Stirling 2016, 17). He concludes that, “By contrast with the technocratic procedures of risk assessment, precaution is about greater democracy under uncertainty” (Stirling 2016, 17).

The application of the Precautionary Principle at the level of project design may discourage some pathways of development, but it would provide researchers with the ethical and responsible principle of channelling alternative routes to scientific innovation and discovery, covering gaps in knowledge and fostering new discoveries. As a necessary stage to responsible technological development, it not only represents a strong commitment to the well-being of the population and systems affected, it also prevents the waste of resources on expensive interventions, lukewarm mitigation strategies and unnecessary and non-useful data gathering, that typically follow when technologies are adopted without due regard to the need to make precautionary decisions in a context of uncertainty. It promotes a scientific pathway that embraces complexity and uncertainty with more humility and less hubris.

The impact of the application of the Precautionary Principle on all technological research would not only favour science and policies regarding health and the environment. It has the potential of reinforcing democratic principles, by rebuilding trust between politicians, scientists and the public. When it comes to gene drives, this implies that alternative trajectories of innovation must be part of the debate, and that consideration of alternatives must occur not only at the point at which GDOs might be released into the environment, but also at very early stages, when research priorities are being set.

8.4 Precautionary Principle for GDOs

When GDOs are the subject of debate, the Precautionary Principle is often invoked, but rarely developed. An example may be drawn from the 2016 National Academies of Sciences, Engineering, and Medicine (NASEM) report “Gene Drives on the Horizon: Advancing Science, Navigation Uncertainty, and Aligning Research with Public Values”. Although the report mentions the Precautionary Principle a few
times, it gives more attention to its technical aspects rather than its ethical, philosophical and political dimensions. For example, it sometimes focuses on the principle as being useful at the stage of testing and environmental release, stating that uncertainties in the case of GDOs are structural to this phase of the technology development. In this matter, the experts contributing to the report promote the idea that a step-by-step assessment is necessary; however, they never question the necessity of developing such technologies in the first place, through applying the Precautionary Principle to research.

The authors also refer to the asymmetries among countries regarding the Precautionary Principle and the instruments available to regulate and govern GMOs. These may pose a barrier when it comes to national cooperation on research and assessment of GDOs, and also create asymmetries of power when it comes to definitions of ethical standards.

Beisel and Boëte note that regulation of GM mosquitoes with self-spreading genetics (such as GDOs), “is considered almost impossible, or at the very least extremely difficult” (Beisel and Boëte 2013, 50). Further, “GM mosquitoes and other public health measures to control malaria will not be able to coexist”, because this strategy actually relies on people fostering the survival and spread of the GM mosquitoes, rather than avoiding and killing them as would normally be the case with other public health measures, such as using bed nets or removing breeding sites (Beisel and Boëte 2013, 53). Beisel and Boëte note that GM mosquito strategies are “particularly vulnerable to unforeseen effects and ecological uncertainties”, (Beisel and Boëte 2013, 53) for example:

- it is unknown how (and how quickly) mosquito and parasite populations would react to the introduction of GM mosquitoes;
- it is unknown how many species would need to be transformed in order to interrupt the transmission of the malaria parasite;
- significant ecological uncertainties are inherent to the complex and shifting disease ecologies of malaria.

These concerns will also apply to other GDOs, not just mosquitoes, due to the intention that they spread and replicate in the environment. In effect, the open release of GDOs is intended to re-engineer whole ecosystems, and therefore the role of the Precautionary Principle is particularly important.

9 Who is liable if anything goes wrong?

Issues of liability are covered by the Nagoya-KL Supplementary Protocol on Liability and Redress, and, in addition, individual states have a responsibility under international law to not cause harm to the environment of another State. However, liability and redress is a critical if still deficient component in the regulatory toolbox. Deficiencies include the long term, irreversible nature of potential harm, and the difficulties in establishing proof of any damage and its source.

In releases of GM insects to date, one concern has been the use of in-country partners (by both Oxitec and Target Malaria) to make the applications to regulators, and the absence of transboundary notifications published by the exporter (see Section 7.3). Depending on whether the developer or the in-country partner is defined as the ‘operator’ in national law, this could mean that the in-country partner is held liable if anything goes wrong, allowing the developer (usually based in a rich country) to walk away and not take the responsibility or bear the costs of any future harm.

The difficulties in establishing liability may be exacerbated by gene drives spreading across national boundaries, with potentially long-term effects.
10 Public engagement

There is recognition by academics working in the field, such as Brossard et al. that “Deciding to use gene drives to control and suppress pests will involve more than a technical assessment of the risks involved, and responsible decision-making regarding their use will require concerted efforts from multiple actors” (Brossard et al. 2019, 1). They recognise that “technical expertise is not enough to address the complexities surrounding a scientific issue that has not only technical but also social, ethical, and legal dimensions” (Brossard et al. 2019, 1). They further note that “Editing pernicious genes to make a disease-causing mosquito, or a pathogen-carrying rodent, less harmful sounds like an appealing idea. But there are serious questions about the ethics of engineering a wild species and about potential environmental consequences that might change ecosystem dynamics or spread well beyond the specific targeted location” (Brossard et al. 2019, 2). Brossard et al. also argue that “Engagement about gene drives should aim to foster open, substantive dialogue between all interested and affected individuals in areas where the technology may be used” (Brossard et al. 2019, 4).

The history of Public Engagement of Science (PES) is vast and it has gone through several changes since it was first proposed by an official scientific/political body at the turn of the millennium (House of Lords Science and Technology Committee 2000). Today, PES is no longer just the ethical responsibility that scientists owe society; it is part of basic research design, expected to bring benefits to scientists’ careers as well as to society. Some argue this is a win-win situation, with the optimistic claim that its theoretically two-way communication between publics and scientists generates mutual understanding and greater trust.

However, because the theory of PES is rooted in a process of sharing and mutual learning, any experience of engagement must be anchored on the premise that society (in its forms of organisation) has “ways of knowing” and also deep concerns that may differ substantially from those of science. In other words, society has methodological and epistemic resources that sometimes may diverge from those used by scientists.

10.1 Alternatives to a ‘pathway for acceptance’?

For a long time, institutions have been defining the wrong questions and making the wrong assumptions when it comes to public engagement. Rather than seeing engagement as a democratic right, most of the initiatives taking place approach the provision of information to the public as primarily an attempt to create a system that does not generate controversy or resistance to scientific and technological outcomes. This means that the goal of public engagement as we know it is not democratic, but simply a ‘pathway for acceptance’, which does not allow for the option of rejecting a particular technology or approach and instead choosing alternative approaches.

This bias of public engagement in science is reflected in some of the initiatives already implemented. For example, it’s not rare to find that the feedback from those engaged in deliberative forums often reflects feelings of disappointment, loss of time and feelings of impotence (PSx2 2008). One of the main reasons people experience these negative feelings regarding their engagement with science is that the apparatus for participation rarely reflects how most people would wish to approach the actual use of the technology. Others may even report exhaustion, especially when people are enrolled in a continuous process of participation that doesn’t produce any achievable outcomes relevant to their own interests.

Stirling (2014) argues that if public engagement exercises around innovation, including gene drives, are to be credible and robust, they should not be restricted to issues of risk or safety alone, nor confined merely to the ways in which a new technology ‘should’ or is expected to work; nor should they assume that the technology will be introduced in any
case, whatever the outcome of the public engagement.

Stirling et al. (2018) discuss risk, participation and democracy in the governance of new synthetic biology and gene drive technologies. They argue (Stirling et al. 2018, 44) that genuine empowerment of all affected parties actually interested in making better choices differs from ‘instrumental’ participation, which is simply about engineering pre-existing aims (such as: fostering trust; providing justification; securing acceptance; and managing blame). Stirling et al. (2018, 44) therefore consider how regulatory assessment of gene drives can move from a purely risk-based analysis to diverse and more substantive processes of ‘social appraisal’.

This same article also emphasises that appraisal should devote symmetrical attention to all practical alternatives and offer a balanced picture of associated pros and cons as seen by the affected stakeholders – particularly those having no commercial interest in the technology under consideration (Stirling et al. 2018, 46). Questions around benefit and harm must be directed to the potential pros and cons associated with a diverse array of alternative policy options. These pros and cons would highlight the importance of embedding risk-based assessment in a broader social appraisal that includes public participation. Real participation must recognise: a.) that some level of ignorance will always exist with a new technology; and b.) that a substantive social appraisal entails value-based judgements that probabilistic risk assessment techniques are not designed to address (Stirling et al. 2018, 48).

Leach et al. (2010) point out that technological fixes frequently fail to work and create further problems because they are most often modelled in labs or on computers, methodologies which do not reflect the complexity of real world situations. These authors argue in favour of offering a broader range of options at such participatory sessions, described as “multiple potential pathways to sustainability”. Such an approach draws attention to the contrast between “dominant” and “alternative” narratives. For example, for infectious disease epidemics, the dominant narrative is that outbreaks are threatening humanity and need to be controlled through surveillance and technological solutions. An alternative narrative might be that “underlying causes need to be tackled, requiring a rethink of surveillance and diverse social, cultural, ecological and technological responses” (Leach et al. 2010, Table 7.3). According to Leach et al. (2010), that would lead to greater recognition of uncertainty and would empower approaches more rooted in local needs that feature more equitable, socially distributed outcomes. They list five key principles for appraisal for sustainability:

- Include a diversity of types of knowledge through participatory engagement;
- Extend scope and enable choice;
- Take a dynamic perspective, accept incomplete knowledge;
- Attend to rights, equity and power; and
- Be reflexive (Leach et al. 2010, Table 5.3).

The dominant versus alternative narrative is clearly visible in the case of GDOs, for example in proposals to release gene drive mosquitoes as a proposed technological solution to tackle malaria, as there are many other approaches that might work better with less risk. Leach et al.’s (2010) five key principles are therefore essential requirements for public engagement to be meaningful.

Ely et al. argue that technology assessment practices can serve to unjustifiably ‘close down’ debate, “failing adequately to address technical uncertainties and social ambiguities, reducing scope for democratic accountability and co-ordination across scales and contexts” (Ely et al. 2013, 1). They note that “existing efforts in technology development and wider innovation are typically most strongly steered by incumbent interests, which often do not match those of the most vulnerable groups, and frequently fail fully to account for social, technical and ecological complexities and uncertainties” (Ely et al. 2013, 1). They argue in favour of “broadening out” and “opening up” technology assessment. By
Chapter 3: Social issues

10.1.1 Need for engagement in the definition of a problem and for ‘broadening out’ societal appraisal

Several aspects of today’s current paradigm of engagement are responsible for the frustrations described above. One is the fact that participation intended to generate acceptance does not engage people in the first place in a clear definition of what the problem actually is for which their assessment is needed. For example, holding a public consultation, as part of gaining authorisation to market new genetically modified crops, may allow farmers to express their concerns regarding the impact of these technologies in their production but it never asks the farmers what actual problems they’re facing in the first place. Problems are, in public engagement of science and technology, defined a priori by the consultation, participation or deliberation spaces, and by the scientists and promoters who have already decided on what they are. The reason for this is that the hegemonic paradigm of participation or engagement sees citizens as objects and not as subjects of the discourse. As Wynne (2003) has described, in contemporary policy culture, it is problematically not ordinary public citizens, but scientific experts who are assumed to be the proper authors of “public meanings” (the accepted meaning of public issues, especially those involving ‘science’, for policy to manage).

This problem has led Civil Society Organisations to call for opportunities for participation to be provided from the very beginning of the process, which would then include the question of how funding for scientific research is allocated (PSx2 2008, 31). In the case of GDOs, this would mean opening up the question of research priorities to much earlier, more in-depth, discussions.

Unfortunately, most of the institutions that fund research promote only a limited forum for engagement. Discussion of what kinds of projects should be considered for a funding call is currently rarely open to the engagement of the affected public. There is a need to recognise that public engagement should be a fundamental part of the preliminary phases; that is, when the whole complex of funders,
innovation stakeholders and researchers engage in an exclusive and elite process in which they pose and develop a question for R&D.

Engaging society in debates about GDOs has many challenges, as does any initiative trying to include public engagement with scientific innovation. These challenges have been identified within the recurrent debates over the impact of new technologies with effects that are highly uncertain. One example, which is also stressed in the NASEM (2016) report, is: which groups should engage in the participatory initiatives of GDOs risk assessment? It is widely recognised that people affected by the technology have a strong interest in being able to join engagement initiatives; but the communities engaging in this participatory process are often vulnerable, that is, at serious disadvantages compared to the researchers and promoters. In the case of GDOs seeking public approval for release that promise to reduce or control an infectious disease, that vulnerability is constructed around the fact that they are the ones being affected by this disease. This fact may of course make such a public more liable to accept technologies that promise to eliminate the disease than those who are not affected. This may not mean they desire the technology, only that they are too vulnerable to oppose it.

Although the idea of public engagement in decision-making is accepted by most of the scientists and experts working in risk assessment with human communities, there is a fundamental bias in their vision of how this should work. They often assume that these communities are inactive regarding the disease concerned. This is often not true, which represents a challenge to mainstream strategies of engagement that mostly begin from the false premise that there are no local risk assessment strategies already being implemented, or that those in existence are based in ignorance and therefore do not serve to address the problem. When considering the engagement of communities, we should not only take into consideration the condition of the scientific research, we also need to engage in debates concerning value and power relations.

Discussing releases of GM mosquitoes intended to tackle dengue, Nading notes that, “Ethics that appeal to risk calculated in nested regulatory institutions, a standardizable body or an idealized ‘nature’, prevent us from asking, ‘What if resources were put toward changing the conditions that make the environments of Grand Cayman, Bahia, Kualalampur and Key West (not to mention less research-ready spaces such as Managua and Manila) dengue-endemic in the first place?’ In other words, these discourses divert our attention from the fact that dengue the disease, like the GM organism that would be its cure, is a product of uneven, though by no means unchanging, political and economic relations” (Nading 2015, 41).

When addressing the scientific questions regarding GDOs, rather than enquiring whether GDOs may cause unintended effects, we should ask ourselves at the earliest stages: ‘How well do we know the diseases we are targeting? How well do we understand the complexity of the ecology of the target populations? Are these diseases only transmitted by certain vectors? Which disciplines do we need to engage in the development of such technologies?’

For example, according to the Target Malaria project, it seems that medicine and public health professionals are not included when these outreach teams are constituted. As we see from their website, the team mostly consists of biologists, geneticists and engineers, with a clear absence of health professionals. Such a team composition seems an odd choice, considering the promises made about these GDOs primarily concern improved human health. Furthermore, as is stressed in the NASEM (2016) report, communities also have their own ‘ways of knowing’ when it comes to these scientific questions, which means we should not only promote the exchange of knowledge, we should incorporate their knowledge in the apparatus of participation, the definition of the questions, the project design and its implementation and periodic review. We should also be prepared to fail; that means that engagement must not be conducted within the premise that the technology will be accepted, that it only needs some small modification and technical instruments for assessment to achieve that invariable goal. We
must be prepared to reject these technologies, not just in favour of alternatives that may already exist, but also in favour of alternative paths of development for the future.

10.1.2 The need for problem-led engagement

A related issue is the need for engagement to be problem-led, not technology-led. One of the major critiques of today’s methods of scientific production of knowledge is that they are mostly oriented in order to serve their internal technological apparatus, rather than to seriously consider a problem or scientific challenge that needs to be addressed.

For example, the NASEM (2016) report reflects this problem. This report, which tried to “create a consensus to summarize the current understanding of the scientific discoveries regarding gene drives” (NASEM 2016, vii), not to mention its subtle contradictions, assumes that problems regarding the impacts that could conceivably be caused by gene drives are mainly to be solved by adapting new versions of the same technology. For example, it’s often highlighted in the report that one possible solution regarding the impact of gene drives is to introduce another genetically modified mosquito (with the as yet non-existent “reversal drives”), even when the authors accept that these, even if eventually perfected, may create impacts of their own.

In contrast, problem-led research is based on posing fundamental questions about a given problem. If we accept uncritically that a technology is the best (or only) solution to complex phenomena such as famine or disease, we will be trapped in the current socio-technological apparatus. As Kloppenburg (2005) has argued, this bias generates a scientific contradiction. The contradiction is simple: the socio-technological bias of modern society (and consequently of modern science) is based on the desire to continuously revolutionise the means of production and consumption. Project applications for funding reflect this essentially economic goal.

Researchers have all faced that blank space in grant application forms, which requires an answer to questions such as: What is the novelty of your approach? Which new products does your research generate? What is the intrinsic value of your project? To these questions only a few will risk answering with “old”, non-technological approaches (such as traditional, indigenous and local knowledge). Researchers tend to ignore them; they are no longer in fashion. The choices we are led to make by a technology-oriented approach makes us ignore tested methodologies built by our own communities. With time, and because research tends to move in the direction of innovation, some of this important knowledge is forgotten. This represents a creative form of destruction of memory and experience, opening a gap of open enquiry within the fabric of the scientific enterprise.

A broader approach would begin with different definitions of the problem that is being investigated (such as the challenge of tropical disease), especially to those problems involving social actors, and a serious consideration of all the alternatives that could be used or developed in order to tackle it, including social measures such as alleviating poverty or lack of access to clean water. In the context of GDOs, this means that public engagement should never begin with the promotion of a claimed technological ‘solution’.

10.1.3 The need to avoid unrealistic promises

As noted above in Section 5, unrealistic promises distort public engagement in debates about new technologies. For credible public engagement to take place, uncertainty about what can be delivered needs to be openly acknowledged and unrealistic promises must be avoided.

If public engagement exercises are framed in a way that implies tremendous benefits are likely (or even inevitable) if open releases of GDOs are permitted, this limits the space for discussion of the complexity of such an approach and its dependence on numerous unverified assumptions. It also does not address the issue of the opportunity costs associated with investing in any approach that might not deliver
the claimed outcomes. Over-hyped claims of future benefits may also prevent some concerns from being included in the framing of the discussion (because, by definition, the gene drive organism is pre-supposed to be successful and therefore any harms associated with its failure are excluded from debate).

Addressing the issue of unrealistic promises also requires new approaches to the governance of science in order to regulate the ‘political economy of promise’ currently shaping scientific culture in the public interest. This has not even been posed as a problem to be addressed, let alone been subject to collective analysis and deliberation.

10.1.4 The need for inclusiveness and responsiveness

Civil Society Organisations have argued that the innovation process needs to be opened up so that all stakeholders have enough time to consider the implications of a new technology (PSx2 2008, 30-32). Everyone should be able to participate at some level and in some capacity; this would necessarily include Civil Society Organisations. Participation needs to be on an equal footing in order to address unequal power relations, and public concerns must be listened to and taken into account (i.e. the process must be responsive).

Due to issues with power imbalances, there is a particular need to include marginalised groups. Furthermore, ‘inclusiveness’ must not mean a simple invitation to speak, but a genuine opportunity to shape agendas, including research agendas, and to affect decisions. This should include a right to refuse to take part in a particular project, and to propose and explore alternative approaches.

The challenges of engagement in debates regarding GDOs are particularly great, due to this technology’s potentially invasive, international and irreversible effects.

10.1.5 Role of scientists and ‘counter-expertise’

Suppression of dissenting scientific voices has long been the norm in science (Martin 1999; Delborne 2016). The goal of this suppression is not just a defence of the rationality of the scientific system. It is equally a professional defence of the curtain of authority and power that separates science from society. That curtain makes sure that the roles for engagement are decided by the field of the “Us”, that is, the protagonists for an innovation, and that the “Others” are the ones who need to adapt in order to participate.

Civil Society Organisations have argued that ‘counter-expertise’ plays an important role in exposing bias and enabling alternative perspectives to be heard (PSx2 2008, 31). However, there cannot be counter-expertise without funding and resources. Transparency and two-way exchanges of information, open-mindedness and genuine engagement are also essential for societal knowledge-development and learning. Debates both within and about science should involve different opinions/viewpoints and a plurality of expertise and recognition of other types of knowledge that take into account minority experiences and voices.

This means that another model of engagement is needed. Some alternatives have been initiated by groups of critical scholars in an interdisciplinary way (e.g. Nunes et al. 2014). These initiatives take into account many facets of society and of its communities and groups, including economic, social and cultural aspects. When a researcher approaches engagement from a critical and self-reflective perspective, mutual learning can take place; the movement of knowledge then becomes a flux and not a linear process. The tools and the apparatus for participation are both built on the people’s forms of organisation and in their values and concerns. However, this effort requires time and resources.
11 Conclusions

In this chapter, we have considered the political economy of GDOs, including how research is patented and funded, and how funding concerns lead to unrealistic claims about what researchers can deliver. Gene drive R&D is still in its infancy and far from any field trials. Many claims about future benefits of gene drives portrayed in media, scientific publications and patent applications thus at best seem premature. Public discussion is often limited to speculative health and conservation applications, with the aim of focusing on those claimed benefits which appear more likely to attract public support.

We have explored how exaggerating effectiveness can lead to opportunity costs when alternative solutions are neglected, and how it can close down public debate about the best ways of developing salient knowledge collectively in order to tackle societal problems.

We then considered how issues such as obtaining prior informed consent have been undertaken by existing projects wishing to release genetically modified (GM) mosquitoes (currently without gene drive, but with some plans to include it in the future); and we noted serious limitations in these approaches. We discussed how power imbalances may affect the regulatory framework and who is asked for their input to decisions. We discussed liability and the Precautionary Principle and finally considered the issue of public engagement in decisions about research and development involving GDOs.

Public engagement has to take place at the very beginning of the process, when funders, innovation stakeholders and researchers define what a problem is and set R&D priorities. We conclude that social issues regarding GDOs can only be addressed by broadening the processes of public engagement with prevailing R&D and commercial interests, and by taking a properly precautionary approach. It is essential to acknowledge the extent of the ignorance and uncertainty embodied in the best of scientific understanding of the complexities of ecosystem and human health responses to the release of GDOs, and thus the unpredictability – and irreversibility – of the future effects of GDO releases. Alternative approaches to tackling problems must be part of public engagement with the scientific, regulatory and science policy debates, including questions about what kinds of research should be funded. Public debate should not be framed by unsubstantiated and unrealistic claims about what gene drives can deliver. Genuine empowerment of all affected parties in the interests of making better choices must not be conducted with the premise that the technology will be accepted and that it only needs some small modification and technical changes to achieve that goal. Society must be prepared to reject these technologies, not just in favour of alternatives that may already exist, but also in favour of alternative paths of development for the future.
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Chapter 3: Social issues


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