THE LEGAL REGULATION OF GENE DRIVE TECHNOLOGIES

Charlotte Elves
Balliol College, Oxford

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ABSTRACT

Gene drive technologies purport to provide a panacea and yet in doing so present unprecedented risks that threaten to change, potentially irreversibly, the way in which we live in the world. Gene drive technologies raise questions about what ends societies ought to seek for their citizens, how they are constituted and how those ends might be attained. Despite this, current discussions surrounding gene drive technologies and their regulation focus almost exclusively on the technical implications.

Drawing on the work of sociologists and STS scholars, this thesis argues that lawyers ought to think critically about the ways in which they go about developing their understandings of new technologies as regulatory objects. Lawyers need to evaluate and scrutinize the knowledge claims with which they are presented, and work to identify those extending beyond the required technical expertise, if the regulatory frames they build are to bear fidelity to the realities of the technology.

This thesis draws out the regulatory disconnection generated by the current regulation of gene drive technologies through the existing European Union GMO regime. It then goes on to describe the ways in which regulatory reconnection might be achieved by constructing broader frames through which we describe gene drive technologies as a regulatory object. In thinking about how lawyers might go about broadening the frames that they build, this thesis takes examples from Public Health Law scholarship and legislation.

In response to both the normative and epistemic lacunae highlighted above, this thesis develops an account of why and how ethical enquiry ought to play a significant role in informing our descriptions of gene drive technologies as regulatory objects.

Furthermore, this thesis argues that ethical enquiry is capable of articulating questions to which technical experts must provide answers if we are to develop fuller understandings of the technologies we regulate. In this way, ethical enquiry can help lawyers bridge both the normative and epistemic gaps that they are so often faced with in the regulation of emerging technologies.

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CHAPTER ONE: INTRODUCTION

In 2017, over 219 million people world-wide contracted malaria. For nearly half a million of those infected, the disease proved fatal.[1] Of those who died, over sixty percent were children under five.[2] Whilst nearly half of the world's population is considered at risk of malaria, it is Africa that bears the greatest disease burden, accounting for over ninety per cent of cases.[3] Besides the very real human cost of malaria, African governments spend in the region of one billion dollars a year in the fight against malaria. Numerous economic studies have demonstrated that in sub-Saharan Africa, the area most affected, malarial disease stunts economic growth, directly contributing to the poverty of the region.[4]

For decades, attempts to control the spread of malaria have focused on controlling the populations of its mosquito vector. Governments have invested in programs of insecticide spraying and the use of larval traps to reduce the numbers of mosquitos living alongside human communities.[5] Other techniques have focused on distributing insecticide impregnated bed nets to protect from being bitten during the night – the mosquito's most active time.[6] A considerable focus has been directed towards developing and making more available anti-malarial drugs as a prophylactic against malarial infection and improving drugs for treatment once the disease has been contracted.[7]

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[1] World Health Organisation, 'Malaria' (World Health Organization International, 18 June 2019) https://www.who.int/malaria/en/ Last Accessed 11th September 2019.
[2] Ibid.
[3] Ibid.
[4] John Luke Gallup & Jeffrey D Sachs, 'The Economic Burden of Malaria' (2001) American Journal of Tropical Medicine and Hygiene 457.
[5] Cara Smith Gueye et al, 'The central role of national programme management for the achievement of malaria elimination: a cross case-study analysis of nine malaria programmes' (2015) Malaria Journal 488.
[6] Alexis R Sexton, 'Best Practices for an Insecticide-treated bed net distribution programme in sub-Saharan eastern Africa' (2011) Malaria Journal 157.
[7] John Zarocostas, 'African Union launches pan-African anti-Malarial Campaign' (The Lancet, 14 July 2018) https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31606-4/fulltext Last accessed 11th September 2019.

For many years, we were coming out on top – mosquito populations were being pushed down, and with them the rates of malarial disease, illness and death.[8] But, with the emergence of insecticide resistance developed by mosquitos and drug resistance developed by their malaria causing parasites, the tide has turned.[9] Once again, the rates of disease and death are increasing year on year.[10]

Every now and again, science and technology take a lunging jerk forward and in doing so place in our hands the means to condemn various plagues and plights to the annals of history. Before Edward Jenner developed the small pox vaccine in 1798, the disease took the lives of 400,000 people every year.[11] The discovery of anti-biotics made surgery and chemotherapeutic treatments for cancer possible, and child birth safer.[12] Now, the development of gene drive technologies promises to make mosquitos, and with them malaria, a historical phenomenon too.[13]

Gene drive technologies provide scientists with a means of altering the genetic make-up of entire species, and rapidly. They work by releasing genetically modified organisms into wild populations. The edited organisms mate with their wild-type counterparts, ensuring that the selected trait is passed to the resulting offspring. The offspring themselves inherit the selected trait and spread it to subsequent generations. In this way, gene drive technologies differ from conventional gene editing techniques

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[8] Sam Jones, 'Global Deaths from Malaria Drop by 47% - but fight hits critical phase' (The Guardian, 9 December 2014) https://www.theguardian.com/global-development/2014/dec/09/malaria-retreat-insecticide-resistance-africa Last accessed 12th September 2019.

[9] For details about the effects of insecticide resistance in mosquitos see: N Liu, 'Insecticide Resistance in Mosqutioes: Impacts, Mechanisms and Research Directions' (2015) Annual Review of Entomology 537. For details of the effects of parasite resistance to antimalarial drug treatments see: Cui Liwang et al, 'Antimalarial Drug Resistance: Literature Review and Activities and Finding of the ICEMR Network (2015) The American Journal of Tropical Medicine and Hygiene 57.

[10] Anne Gulland, 'Countries Hardest Hit by Malaria See Rise in Cases' (The Telegraph, 19 November 2018) https://www.telegraph.co.uk/global-health/science-and-disease/countries-hardest-hit-malaria-see-rise-cases/ Last accessed 12th September 2019.

[11] Harry Bloch, 'Edward Jenner (1749-1823): The History and Effects of Smallpox, Inoculation and Vaccination' (1993) JAMA Pediatrics 772.

[12] Rustam I Aminov, 'A Brief History of the Antibiotic Era: Lessons Learned and Challenges for the Future' (2010) Frontiers in Microbiology 134.

[13] Heidi Ledford and Ewen Calloway, "Gene Drive' Mosquitoes Engineered to Fight Malaria' (*Nature News*, 23 November 2015) https://www.nature.com/news/gene-drive-mosquitoes-engineered-to-fight-malaria-1.18858 Last accessed 12th September 2019.

insofar as they guarantee that future generations inherit the selected trait. In a relatively short period of time, the selected trait is carried by all individuals within the population. What effect this has depends on the characteristics of the trait selected. For example, some gene drives affect sex selection, ensuring that the genotype inherited by subsequent generations is the coding for male sex. In that way, the gene drive ensures that only male offspring are born, and in time the population crashes completely for lack of viable mating pairs.[14] Other gene drive cause the biased inheritance of the genotype coding for parasite resistance.[15] Within a relatively short period of time, that gene drive ensures that a vector population is prevented from carrying and spreading disease. As such, gene drives spread genetic changes through a population rapidly, and in a potentially irreversible fashion.

In this way, gene drive technologies are quite different to scientific and technical advances such as the smallpox vaccine described above. The unprecedented opportunities they present do not come without risk. Some of these risks are recognized, others uncertain and some are altogether unknown. Altering the genetic make-up of entire species, or even eradicating them entirely, has the potential to change the world as we presently live in it. Gene drive technologies and their use have implications not just for individuals, but for whole populations. Gene drive technologies will operate at scale, distributing both benefits and burdens across entire societies or, in the case of the most prolific gene drive-systems, entire continents, and their effects are potentially irreversible.

Gene drive is a technology that confronts us with questions about the ways in which we live in the world. Gene drive technologies raise questions about what ends

[14] Valentino M Gantz and others, 'Highly Efficient Cas9-Mediated Gene Drive for Population Modification of the Malaria Vector Mosquito Anopheles Stephensi' (2015) 112 Proceedings of the National Academy of Sciences E6736 <http://www.pnas.org/lookup/doi/10.1073/pnas.1521077112>. Last accessed 7th September 2016.
[15] Andrew Hammond and others, 'A CRISPR-Cas9 Gene Drive System Targeting Female Reproduction in the Malaria Mosquito Vector Anopheles Gambiae' (2016) 34 Nature Biotechnology 78.

societies ought to seek for their citizens, how they are constituted, and how those ends might be attained. Further, and quite unlike the smallpox vaccine and the development of antibiotics, identifying those whose interests might be affected by the technological development, and who might be responsible for those interferences, is a complex task. Present understandings of gene drive technologies do little to help answer questions about the benefits or burdens that they bring and who it is that will come to bear those benefits and burdens.

1. Beyond the Technical: The Basic Argument of the Thesis

Despite the complex range of ethical questions that they raise, thinking about gene drive technologies, their use and how we ought to regulate them has, to date, been limited to technical enquiry only. 'Technical solutions', 'technical challenges' and 'technical expertise' are referred to regularly throughout this thesis, and oftentimes, criticisms are levelled at decision-making based purely on a technical understanding of gene drive technologies and the world around us. What then, does 'technical' denote? The Oxford English Dictionary defines 'technical' as follows:

> Of a person: having knowledge of or expertise in a particular art, science, or other subject; skilled in the formal and practical techniques of a particular field. In later use chiefly: expert in or concerned with applied and industrial sciences.[16]

The usage throughout this thesis does not depart far from the ordinary language meaning cited above. Technical here refers to those knowledge claims or understandings derivable only through the analytical methodologies of various scientific disciplines and intelligible only to those well versed in those disciplines and methodologies. In this way, I use the term 'technical' in much the same sense as Theodore Porter, who describes technical claims as those knowledge propositions that exist beyond the domain of public reason.[17] For Porter, technical expertise can be

[16] 'technical, adj. and n.' (OED Online, OUP June 2009) https://www.oed.com/view/Entry/198447?redirectedFrom=technical#eid Last accessed 12th September 2019.
[17] Theodore Porter, 'How Science Became Technical' (1998) Isis 292, 296

characterized by inaccessible, specialist language and methodologies, and their claims to objectivity and reason.[18] However, as Porter notes, technical considerations can, and very often do, have implications that extend beyond the confinements of objectivity, spilling out with consequences that very much are, and ought to be, within the domain of public reason.[19] Despite this, appeals to technicality have a siloing effect, banishing all matters considered technical away from non-expert gaze, for consideration by specialists only.

Borrowing from Steven Shapin, we trusts scientists and the technical expertise that they put forth for the same reason we trust mechanics to fix our cars – not because of their superior rationality but because they have the skills to do the work, whilst we do not.[20] Porter, extending the analogy further, asks:

> What can we trust these specialists to do? We would not put too much stock in the opinion of our mechanic that, since a car in good working order can easily drive right across national boundaries, there is no alternative for the European Union but to ratify a unified constitution and for other continents to follow the same model. The technical specialist, like the mechanic, knows how to do a particular job—and apart from that has opinions like everyone else.[21]

In that sense then, the technical expertise surrounding gene drive technologies tells us a lot about what we can do, and what it possible: that certain gene-editing techniques can be put to certain uses, in certain ways, creating various different world states. Mosquitos can be genetically manipulated to end malaria. Mice might be altered to eradicate Lyme disease. In this sense, we understand technical expertise to advance propositions about what we can do and what might be possible, but it provides little assistance in determining what we should do. Furthermore, technical expertise can only tell us what it knows – and so much of what we need to know cannot be captured, understood or articulated by technical expertise alone.

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[18] Ibid 293.
[19] Ibid 293.
[20] Ibid 296.
[21] Steven Shapin, The Social History of Truth: Civility and Science in Seventeenth- Century England (University of Chicago Press, 1994).

Oftentimes, technical descriptions of a phenomena or problem are appealing for lawyers and those responsible for the promulgation of regulation. This in itself is not a novel observation – scholars have, for some time, noted the lawyer's inclination toward technical expertise as the primary ground for regulatory decision making. For instance, lawyerly reliance on technical expertise has been noted by Elizabeth Fisher in her description of the rational-instrumental paradigm of regulatory decision making.[22] Under the rational-instrumental paradigm, our understandings of technologies and their place in the world are limited to propositions or claims that can be evidenced or tested by analytical methodologies and objective science.[23] Understandings are constrained by reductionist representations of complex phenomena. Thus, the rational-instrumental paradigm paints a picture of technologies within which their characteristics and consequences are observable, measurable and predictable. Any uncertainties that the technologies do present can be controlled and managed. For lawyers, as Fisher states, technical expertise often provides an understanding of complex problems within which they can be quantified and controlled with confidence.[24] In this way, through appeals to objectivity, the risks associated with novel technologies appear manageable, and as though they might be adequately contained by the regulatory frameworks put forward.[25]

In the context of gene drive technologies, we see the privileging of technical representations espoused in claims that the effects of the technology and its safety can be accurately determined through understandings of the organism's generation times, population dynamics and molecular biology.[26] Perhaps the most obvious

[22] Elizabeth Fisher, Risk Regulation and Administrative Constitutionalism (Hart Publishing 2009) 28-30.
[23] Ibid 29.
[24] Ibid 30.
[25] T Porter, Trust in Numbers: The Pursuit of Objectivity in Science and Public Life (Princeton, Princeton University Press, 1995).
[26] National Academies of Science, Engineering and Mathematics Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct, 'Gene Drives on the Horizon:

demonstration of the dominance of technical thinking were the suggestions that should the release of a gene drive cause problems or behave in unexpected ways, the solution would be to release another gene drive designed to reverse the effects of the first, errant drive.[27] The insistence that any harms caused by gene drive technologies might be halted and even reversed by the further release of a gene drive rests on the assumption that all of the relevant features of the technology and the receiving environment are observable and quantifiable to the extent that we can know precisely how to design a successful reversal drive.

Furthermore, in the little existing literature that does exist, assumptions about the sort of knowledge required in order to assess whether or not a given gene drive application ought to be pursued are confined to technical claims derived from 'objective' analytical methodologies. For instance, a recent article that sets out to identify current knowledge gaps in risk assessment and risk management focuses only on furthering understandings of genomic sequences, gene flow, reproductive capacities and other analytical claims.[28] No attention is paid to building understandings of how human communities might interact with the technology affecting either the way the technology works beyond the controlled confines of the lab, or how those human communities might be affected. In this way, it is clear that present thinking about gene drive technologies excludes those knowledge claims proffered by anything other than technical expertise.

To be sure, placing technical expertise at the centre of regulatory decision-making is not always a misstep. A good number of technologies and/or practices about which we have to make difficult decisions are constituted in such a way that deriving

Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' (Washington: National Academies Press) 144.

[27] Ibid 91.

[28] Dorian Moro and Margaret Byrne *et al*, 'Identifying Knowledge Gaps for Gene Drive Research to Control Invasive Animal Species: The Next CRISPR Step' (2018) Global Ecology and Conservation e00363.

conclusions about how they might be regulated from technical expertise is the correct approach. In certain contexts, subjecting a given phenomenon to the demands of quantification and control is precisely the model of decision making that provides the safety and fairness that I argue is currently lacking in the gene drive context. For example, in making decisions about whether or not new drug therapies are safe enough to market, decision-making predicated on the scientific findings proffered by technical expertise is the best option. In the pharmaceutical context, where uncertainty is low, systems closed, and effects are observable, measurable and predictable, making decisions on the basis of the evidence yielded by analytical methodologies ensures the safety that we demand. The nature of the processes and technologies deployed in the research and development of pharmaceuticals renders it amenable to effective regulation deploying the rational-instrumental paradigm. As such, I am careful to make sure that the thrust of this thesis is not about condemning the use of scientific findings and technical expertise in regulatory decision-making, but merely asking that we pause to consider their appropriate role and reach and, where necessary, recognize and respond to their limitations.

Limiting discussions of gene drive technologies to the offering of technical expertise alone has a number of troublesome consequences. In the first instance, technical discussions ignore the normative implications of the technology. Recalling Porter, exclusive focus on matters of technical expertise fails to recognize those technological innovations that spill out over the confines of the technical to present real and pressing challenges in the domain of public reason.[29] Whilst the molecular mechanisms required to eradicate entire populations quite understandably exist

[29] Porter (n25) 308.

beyond the domain of public reason, the effects of eradication should fall squarely within it.

Secondly, conceiving of gene drive technologies merely as a technical solution to a technical problem fails to identify a range of harms that the technology might bring to bear, as well as the range of persons affected. Thus, whilst technical expertise is, doubtless, vital to the ways in which we come to understand new technologies for the purposes of regulation, it cannot be the sovereign voice.

In response to both the normative and epistemic lacunae discussed above, this thesis develops an account of why and how ethical enquiry should play a significant role in discussions about how we regulate gene drive technologies. Not only can ethical enquiry ensure that the world states brought about by new technologies are fair in a way that technical expertise alone cannot, it can also play a role in bridging the epistemic gaps with which we are so often faced in regulating new technologies.

1.1. On Limits and Limitation

There are some things that I chose not to do in this thesis, and others for which there is simply not the time or space. As such, it serves at the outset to tell the reader what the thesis is not about – where it draws its outer limits. Anyone leafing through these pages in search of a neat road map that finds at its destination a ready to go framework for the regulation of gene drive technologies will close the back cover disappointed. Instead, this thesis does the necessary work antecedent to drafting regulatory regimes. It provides the starting point from which thinking about the apt regulatory responses can begin. It challenges lawyers to reconceive the way that that they go about understanding complex technologies. As such, this thesis aims to equip lawyers thinking about the regulation of gene drive technologies with the questions that they ought to ask, rather than furnish them with a handbook of answers.

Secondly, this thesis only focuses on one subset of applications for gene drive technologies. Whilst a number of applications of gene drive technologies, ranging from conservation to agriculture, were noted above, this thesis focuses on gene drive technologies for public health purposes - the eradication of malaria in particular. There are two reasons why I limit the discussion in this way. In the first instance, I suggest that gene drive technologies for conservation, pest control or agriculture ought to be treated as regulatory objects distinct from gene drive technologies used for public health purposes. This is because the questions that we must ask, and the choices that we have to make with regards to the use of gene drive technologies for these other purposes are quite different. To that end, lumping together all instances and applications of gene drive technologies and their regulation would run counter to the very aims of this thesis. In imploring lawyers to think carefully about how we understand novel technologies instead of relying on pre-existing frames and technical expertise alone, it is incumbent on me to lead by example.

However, precluding these other applications of gene drive technologies from the analysis pursued in the proceeding chapters also rests on substantial ethical presupposition. Given the uncertainties surrounding the extent of benefits and burdens that gene drive technologies might distribute, I have taken the view that only the most necessary applications of gene drive technologies ought to be contemplated. Put simply, rolling the dice on the use of an uncertain and risky technology can only find ethical justification in the face of the direst circumstances.[30]

1.2 Defining 'Lawyers'

Before we can begin in earnest however, there is some definitional housekeeping that ought to be taken care of. Throughout this thesis, 'lawyers' are put to regular use.

[30] Katherine V Kortenk AMP and Colleen F Moore, 'Ethics Under Uncertainty: The Morality and Appropriateness of Utilitarianism When Outcomes Are Uncertain' (2014) The American Journal of Psychology 367.

Within this thesis there are regular calls for lawyers to engage in the framing of regulatory objects, for lawyers to take epistemic responsibility, for lawyers to direct choice in co-production. Who then, are these much put upon bunch?

In some ways, I use the term 'lawyers' in a deliberately ambiguous fashion. This ambiguity of usage reflects the wide range of legal actors who influence the direction of the often long and winding path that connects new technologies with the legislative regimes that regulate them. In making regulation, a vast range of individuals with legal training contribute to the ways in which debates are shaped and choices are made about how best we regulate this or that technology. As such, 'lawyers' here refers to all those legal actors involved in the pre-regulatory and regulatory process. Admittedly, this process is, in itself, hard to define – starting somewhere in amongst the meetings and conferences of various domestic and international bodies. For the purposes of this thesis, then, 'lawyers' includes legal scholars and parliamentary counsel, but it also encompasses a more diffuse range of legal actors. The responsibilities outlined in this thesis extend to those legal counsel for Non-Governmental Organizations who make interest representations in regulatory fora and lobbyist lawyers that do likewise.

Defining 'lawyers' this way also has particular temporal implications. In the context of the relation between time, regulation and technology, Roger Brownsword notes that:

> Technology is capable of leaving the law behind at any phase of the regulatory cycle—before regulators have anything resembling an agreed position, before the terms of the regulation are finalized, and once the regulatory scheme is in place.[31]

Directing my argument at lawyers defined in the way I have means that my argument has most traction, and is most applicable, at the very beginning of the regulatory cycle Brownsword describes. In that way, the arguments about the framing I make

[31] Roger Brownsword, Rights, Regulation and the Technological Revolution (Oxford University Press, 2008) 162.

throughout this thesis and the questions I argue lawyers ought to ask in developing an understanding of the technologies they regulate ought to operate at the point in time that there exists no settled regulatory consensus. Thus, I argue that the choices I implore lawyers to make must be taken at a point some distance prior to the drafting of the regulatory letter.

2. The Structure of the Thesis

In the Chapters that follow, I argue that the frameworks considered suitable for the regulation of gene drive technologies are incapable of controlling the benefits and burdens that gene drive technologies might bring with them, because they fail to recognise the novel challenges that this new technology brings. As such, this thesis sets out to demonstrate that if we are to develop regulation capable of accounting for, and where necessary, controlling the benefits and burdens that gene drive technologies present, the range of questions that we ought to ask must be extended beyond those resolvable by scientific evidence and analytical methodologies. In developing an account of how ethical enquiry might revitalize and hone lawyerly thinking in respect of emerging technologies, this thesis takes the following structure.

Chapter Two provides the reader with an overview of the current understandings of gene drive technologies as held by those with an interest in its use and regulation. For the most part, this is a descriptive exercise, referring the reader to the little that has already been written about gene drive technologies and equipping them with all that they need to know in order to make sense of the discussions that follow in later Chapters.

The overview of gene drive technologies that I provide in Chapter Two is derived from the views and understandings espoused in a range of publications from journal articles to policy papers. The thrust of this thesis focuses on how we ought to frame new technologies and a necessary part of that argument demands that we think

critically about what knowledge claims have historically taken precedence in dictating those aspects of a technology we consider relevant and those that fall by the regulatory wayside. In that way, I have sought to ensure that the picture I present is representative of that material as it exists, not one subjected to the editorial discretion of an author with a frame in mind. As such, the information about gene drive technologies and the record of current debates provided in Chapter Two does not represent only the information that I consider relevant, but instead the totality of the discourse as it currently exists. What emerges is an understanding of gene drive technologies that is built, almost exclusively, on technical expertise.

Chapter Three moves on to providing an argument for how and why the way in which we frame new technologies has practical implications for the way that we go about regulating them. In this respect, Chapter Three draws heavily on the work of sociologist Michel Callon. Callon's work animates the thread running throughout this thesis providing both a methodology, but also the language for articulating some of the complex challenges that gene drive technologies present us with. This Chapter therefore reflects on the ways in which we frame certain phenomena, and how these frames get built. At this point, the thesis pivots from talking about the harms, hazards, benefits and burdens of gene drive technologies and instead adopts Callon's language of 'overflows'.[32] Importantly, this move brings with it the ability to discuss complex phenomena without bringing along problematic and contested concepts of risk. In particular, I draw on Callon's account of framing and 'hot situations' in order to highlight the ways in which we might begin to develop proper understandings of gene drive technologies.[33]

[32] Michel Callon, 'An Essay on Framing and Overflowing: Economic Externalities Revisited by Sociology' (1998) The Sociological Review 244.
[33] Ibid.

Vital to the argument in Chapter Three is demonstrating that those in the business of regulating emerging technologies have greater choice in and control over the way in which technologies are framed than might otherwise be appreciated. In this way, Chapter Three builds the argument for eschewing narrow, technical frames, in favour of broader frames – highlighting the ability of these broader frames to identify overflows and agents that otherwise go overlooked.

Chapter Four puts the discussion in Chapter Three to work in the context of gene drive technologies. As such, it provides evidence that the frame constructed by the EU Framework for the regulation of GMOs is too narrow to accommodate the range of overflows and agents affected by the use of gene drive technologies. As such, I argue that the frame constructed in order to understand how best to regulate GMOs bears little fidelity to the realities of gene drive as a regulatory object.

Chapter Five demonstrates the ways in which lawyers might go about broadening the frames that they build. As such, Chapter Five draws on an area of law where the frames constructed have been sufficiently broad as to bear fidelity to the phenomena that they regulate. To that end, this Chapter takes up the example held out by various pieces of public health legislation, demonstrating that technologies can and have been conceived of as something more than technological solutions and thus broader frames, faithful to the technology, its uses and its implications, can be built. This Chapter begins to introduce the role that ethical enquiry played in broadening out regulatory frames and the way in which it is a vital tool in the lawyer's tool kit.

Chapters Six and Seven provide an illustration of the two ethical enquiries that ought to frame the way we think about gene drive technologies. In this way, I highlight how each of these ethical enquiries identify overflows that go overlooked when we build our frames with technical expertise alone. In doing so, I highlight that ways in

which substantive ethical enquiry can play a role in bridging some of those troublesome epistemic gaps but also ensures fairer outcomes.

Chapter Six does two things. In the first instance, it seeks to provide some conclusions about the ethical qualities of both population alteration and population replacement drives, focusing in particular on whether there might be any intrinsic moral prohibitions on the use of gene drive technologies. Secondly, this Chapter goes on to discuss the ways in which the ethical questions explored might play a role in identifying overflows and target agents affected by gene drive technologies. I further consider the ways in which the questions that these ethical enquiries ask might inform technical understandings of gene drive technologies.

Chapter Seven explores the ways in which ethical enquiry shines a light on the ways in which humans might be affected by the use of gene drive technologies, beyond the narrow ascriptions of harm to health currently taken account of. As such, I argue that exploitation ought to be considered a relevant harm when it comes to understanding the ways in which gene drive technologies work, the overflows that they generate and how they ought to be regulated. I describe the conditions under which the use of gene drive technologies might constitute exploitation and highlight the ways in which efforts to avoid exploitation can make the use of gene drive both safer and fairer. Further, I make the case for considering the human communities affected by gene drive technologies as human research subjects for the purposes of regulation.

2.1 Conclusion

Much of the existing literature assumes that the benefits and burdens of gene drive technologies can be totted up on a utilitarian balance sheet, the bottom line of which will tell us what we ought to do. This thesis argues that one of the most challenging aspects of trying to regulate gene drive technologies is accurately identifying and articulating the harms and benefits that regulation should seek to avoid or control and

furthermore, who it is that regulation should be concerned to regulate and who it is regulation should be concerned to protect. I argue that the current understandings of gene drive technologies, informed by technical expertise alone, can never help us to answer these questions. Instead, I argue that we, as lawyers, must reflect carefully on the ways in which we think about these problems. We must think critically about the knowledge claims that we are presented with, and the knowledge claims that we *need* in order to develop true accounts of the technologies that we are tasked with regulating. I argue that ethical enquiry ought to play a considerable role in helping lawyers to build broader frames, capable of bearing fidelity to the technologies that they regulate and the complexities that those technologies present. Only through embedding substantive ethical questions into the ways in which we come to understand these technologies can we hope to build a complete picture of the ways in which they change our world, which communities they affect, how and why.

CHAPTER TWO: WHAT ARE GENE DRIVE TECHNOLOGIES?

This Chapter describes the state of current understandings of gene drive technologies as advanced by those with either technical expertise or some regulatory interest. This Chapter then, does three things. The first section provides the reader with an overview of gene drive technologies - how they work, how they are designed and what some of their implications might be. In this way, the reader is equipped with the technical understanding of gene drive technologies necessary to set up the discussions found in later Chapters.

The second section provides an overview of a range of developments in gene drive technologies and their use. I provide an overview of the scientific and technological progress as a means of developing a narrative that describes the way that the technology is advancing and therefore the choices that are being made in the absence of an adequate regulatory framework.

Finally, I provide an overview of the way that the technology has been discussed and described in the publications of various governments and non-governmental organizations. In doing so, I provide an analysis of the ways in which the technology has been represented in discussions about how best it might be regulated.

Laying out all of the information provided below has presented its own methodological challenge of sorts. This thesis focuses on the way that we think about novel technologies, challenging lawyers to think critically about how and why our present understandings are structured the ways that they are, and how they might be built with greater fidelity to technologies as they actually exist. In this respect, making determinations about the information that we ought to draw on, its provenance and its relevance, is vital to the very exercise I am advocating for.

As such, in presenting the necessary information below, there is a risk that I, as author, might make those determinations on the readers behalf. In writing this Chapter, I could decide what information is relevant to the ways that we think about gene drive technologies, including those sources and voices I consider important and in doing so omit or side-line those that I find to be less helpful or less relevant. Beyond deliberate inclusion and omission for strategic purposes (for

instance, cherry picking the information supportive of the argument that the author makes), authors must also contend with administrative constraints – a chapter can only be so long, word counts are not unlimited and time is not unending.

In as far as it is possible to do so, I have, in this Chapter, sought to present the reader with the totality of the discourse surrounding gene drive technologies as it exists in the literature. Where this has not been possible for reasons of time or space, I have sought to bring any acts of deliberate omission to the reader's attention and direct them to the places in which they might find further elaboration of the issue. As such, this Chapter is not about providing the reader with a ready-made frame with which gene drive technologies might be made sense of, but instead seeks to provide the reader with all the nuts and bolts necessary for constructing that frame. Prescribing which nuts and bolts ought to be used and how they all fit together is the concern of future chapters.

1. What Are Gene Drive Technologies?

Mendelian rules of inheritance dictate that an organism's offspring will have a 50% chance of inheriting a gene from one or other of its parents. This 50% probability of inheritance remains stable across generations as does, on average, the frequency of a particular gene within the population. 'Gene drives' are systems that can produce an exception to these conventional rules of inheritance by stimulating *biased* inheritance of genes. As a result, the offspring of an organism will have a greater than 50% chance of inheriting a gene; how much greater depends on the type of gene drive system used, but recent developments in molecular biology have made possible a 100% rate of inheritance.

With gene drives, the molecular mechanisms for stimulating this biased inheritance are retained within each generation, facilitating the ability to increase the frequency of a gene in a population over successive generations. As such, gene drives, as their names well suggests, provide us with a means of manipulating an organism's genome in order to 'drive' a selected trait through an entire population.

It is in this way that gene drive technologies are quite different to conventional gene-editing technologies. Whilst we have been able to effect genomic alterations in a variety of species for quite some time, conventional techniques have been unable to ensure that all of the modified organism's offspring will inherit the genetic change we effect. As such, traditional gene editing techniques have been limited to altering the genome of one single organism at a time. In simple terms, gene drive technologies present an opportunity to alter the course of evolution in entire populations and for a variety of purposes. It is for these reasons that one of the scientists at the vanguard of gene drive research describes his own work as seeking to 'sculpt evolution'.[1] In this way, gene drive technologies are quite unlike the innovations in gene editing that we have previously encountered. Gene drives can and will spread genetic changes across entire populations, beyond the control of the humans selecting the genetic change, with potentially irreversible consequences.

However, gene drives are not only a product of human artifice. They can occur in nature too; the *Medea* drive in flour beetles being just one example.[2] However, this thesis focuses on engineered gene drive systems, developed by scientists in laboratories. As such, it seems that a working definition can be fixed as follows:

> An engineered system, often based on naturally existing 'selfish' genetic elements that function by increasing in frequency with each generation, even without conferring a fitness advantage upon their hosts, thus forcing non-Mendelian patterns of inheritance.

The challenge is that risks associated with gene drive technologies are inextricably bound up in their virtues. It is the ability of a gene drive technologies to spread themselves across populations that makes them a potentially global solution to malarial disease. However, it is the uncontrollable self-spreading nature of the technology that presents the risk of ecological catastrophe. Furthermore, gene drive technology presents itself as a single use and therefore cheap solution to

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1 'Sculpting Evolution: Exploring Evolutionary and Ecological Engineering' https://www.media.mit.edu/groups/sculpting-evolution/overview/ Last accessed 25th September 2019.

2 M J Wade, & R W Beerman, 'The Population Dynamics of Maternal Effect Selfish genes' (1994) *Genetics* 1309

various different ills, but with its single use nature comes the potential irreversibility of any harms that it might occasion.

2. Types of Gene Drive

Engineered gene drive systems were proposed over a decade ago by Austin Burt.[3] Burt's system was built using natural 'selfish' homing endonuclease genes (HEGs). Since Burt developed his HEG drive, other types of drive have been developed, including sex linked meiotic drives,[4] Medea drives,[5] under-dominance drives,[6] and *Wolbachia* drives.[7] After the development of Burt's initial engineered gene drive, interest in the technology waned. Oftentimes, the drives were unable to drive inheritance at a rate much higher than expected mendelian inheritance. Furthermore, even where the rate of drive was significantly higher, it was often found that the genetic modification made conferred a fitness cost on the target organism causing the selected modification to drop out of the gene pool. As such, early gene drive technologies were not particularly effective at bringing about persistent, population-level change because they could not effectively spread the selected gene throughout the target population. Early gene drive technologies could not be put to any obvious use, being both unreliable and ineffective and as such failed to present any novel regulatory challenges.

However, in 2015 a team working with the only recently discovered CRISPR-Cas9 gene editing system found a way to ensure that the selected genetic change would be inherited by 100% of the edited organism's offspring.[8] Furthermore, the CRISPR-Cas9 gene-editing system also ensured that the trait selected for would be inherited by all individuals in subsequent generations.

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[3] Austin Burt, 'Site-specific selfish genes as tools for the control and genetic engineering of natural populations' (2003) *Proceedings of the Royal Society* 921-928.

[4] Y Huang, K Magori, L Lloyd & F Gould, 'Introducing desirable transgenes into insect populations using Y-linked meiotic drive - A theoretical assessment' (2007) *Evolution* 717.

[5] M J Wade, & R W Beerman, 'The Population Dynamics of Maternal Effect Selfish genes' (1994) *Genetics* 1309.

[6] K Magori & F Gould, 'Genetically engineered underdominance for the manipulation of pest populations: a deterministic model. (2006) *Genetics* 2613.

[7] Austin Burt, 'Heritable Strategies for controlling insect vectors of disease' (2014) *Philosophical Transactions of the Royal Society of Biological Sciences* 20130432.

[8] Valentino M Gantz and others, 'Highly Efficient Cas9-Mediated Gene Drive for Population Modification of the Malaria Vector Mosquito *Anopheles Stephensi*' (2015) 112 Proceedings of the National Academy of Sciences E6736 <http://www.pnas.org/lookup/doi/10.1073/pnas.1521077112>. Last accessed 7th September 2016.

Unlike their forbears, these CRISPR-Cas9 gene drive systems presented the opportunity to spread a selected gene throughout an entire population, permanently and irreversibly.

Since the development of CRISPR-mediated gene drive by Gantz and others, there has been a significant uptick in the rate of gene drive research. A description of how research and policy for gene drive technologies has developed since 2015 is discussed below. Whilst the intricacies of the molecular mechanisms unique to each type of drive will not be explored here, it is important at this point to note that the range of techniques available for building a gene drive does have implications for the regulation of this technology – this point will be returned to in Chapter Four. In short, the molecular mechanism used for building a gene drive matters for two reasons. In the first instance, at least one of the techniques produces a gene drive without effecting a 'genetic modification' as defined in various regulations, including the European Union GMO regulation discussed in Chapter Four. As a consequence, those gene drive technologies are without applicable regulation entirely. Secondly, because the various techniques build gene drives of varying efficiency, whilst the different types of gene drive present benefits and burdens of a broadly similar nature, the magnitude and likelihood of both benefit and burden vary greatly. Put simply, the benefits and burdens distributed by a highly effective CRISPR-Cas9 drive system are quite vast compared to a less effective gene drive built using conventional editing techniques.[9] How legal regulation might conceptualize and respond to these varying degrees of benefit and burden is picked up throughout this thesis.

2.1 Population Alteration versus Population Suppression Drives

In 2015, Gantz and others reported on the first successful laboratory-based proof of principle for a CRISPR/Cas9 gene drive modifying the mosquito, *Anopheles stephensi* (a common vector for the malaria parasite, *Plasmodium falciparum*).[10] Gantz and others demonstrated they could build a gene

[9] Bruce Webber, S Raghu and Owain R Edwards, 'Opinion: Is CRISPR-based gene drive a biocontrol silver bullet or global conservation threat?' (2015) *Proceedings of the National Academies of Sciences* 10565-10567.
[10] Valentino M Gantz and others, 'Highly Efficient Cas9-Mediated Gene Drive for Population Modification of the Malaria Vector Mosquito *Anopheles Stephensi*' (2015) 112 Proceedings of the National Academy of Sciences E6736 <http://www.pnas.org/lookup/doi/10.1073/pnas.1521077112>. Last accessed 7th September 2016.

drive capable of conferring resistance to the *Plasmodium* parasite. In theory, this meant that Gantz's team could build a gene drive that would render a sub-species of mosquito resistant to the malaria-causing parasite and therefore prevent it from spreading the disease.

Some months later Hammond and others published a paper detailing a successful gene drive targeting female reproduction in a different malaria mosquito vector, *Anopheles gambiae*.[11] In theory, the gene drive built by Hammond and others could cause all offspring of gene drive organisms to inherit the genes coding for male sex. In turn, an overabundance of males within the population would, in time, lead to the total eradication of this vector species.

Whilst both systems would cause a reduction in the transmission of malaria and thus reduce the rates of disease, they do so via different techniques. Gantz and others system has become known as a 'population alteration technique'. Population alteration drives change a selected genotype within a population, conferring some or other trait that might not usually be present within the species. By contrast, Hammond and others system is known as a 'population suppression drive'. Population suppression drives usually interfere with fertility or reproductive processes. Hammond's drive, for instance, reduces population size by driving 'maleness' through the wild-type population, thereby disrupting the frequency of reproduction.

Whilst both gene drive techniques are designed to achieve the same result (disease reduction), the threats they pose to human health, the environment and ecology can differ – although that is not to say that there are not threats common to both techniques. For instance, population suppression drives may, in the case of highly efficient gene drive systems, result in the eradication of entire species. The adverse effects that commentators have suggested might follow from a gene drive release are discussed below.

[11] Andrew Hammond and others, 'A CRISPR-Cas9 Gene Drive System Targeting Female Reproduction in the Malaria Mosquito Vector *Anopheles Gambiae*' (2016) 34 *Nature Biotechnology* 78.

2.2 Proposed Applications of Gene Drive Technologies

These engineered gene drive systems have a wide range of proposed potential applications. In the agricultural and environmental contexts, invasive species control and pesticide resistance management are the most likely.[12] However, it is the human health applications that have attracted the most interest to date, both within the scientific community and the mainstream media, with various theoretical proposals for drives designed to control and reduce vector-borne disease.[13] One gene drive pioneer, Kevin Esvelt, argues that gene drive technology has the potential to merge the fields of genomic and ecological engineering, providing solutions to environmental, agricultural and human health challenges.[14]

Current proposed applications of gene drive technologies range from vector control for the purposes of public health to invasive species for the purposes of conservation. For conservation, scientists have suggested that gene drives might be used to remove non-native species from eco-systems in order to restore populations of native species.[15] For example, plans have been tabled for a gene drive designed to restore populations of the Hawaiian Honey Creeper bird.[16] As time moves on, there is increasing discussion of agricultural applications of gene drive technologies, whether for the control of weeds or keeping insect pests at bay.[17]

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[12] Jackson Champer, Anna Buchman and Omar S Akbari, 'Cheating Evolution: Engineering Gene Drives to Manipulate the fate of Wild Populations' (2016) *Nature Reviews* 146, 147.

[13] Esvelt et al, 'Concerning RNA-guided Gene Drives for the Alteration of Wild Populations' (2014) eLife e03402; Oye et al, 'Regulating Gene Drive' (2014) *Sciencexpress* 1254287. For mainstream media representation see: Michael Specter, 'Rewriting the Code of Life' *New Yorker* (New York 2 Jan 2017) http://www.newyorker.com/magazine/2017/01/02/rewriting-the-code-of-life Last accessed 10th May 2017; Chelsea Harvey, 'This new gene technology could wipe out entire species – to save others' *The Washington Post* (Washington 7 September 2016) https://www.washingtonpost.com/news/energy-environment/wp/2016/09/07/this-new-gene-technology-could-wipe-out-entire-species-to-save-others/?utm_term=.7ea07231285c Last accessed 10th May 2017; --, 'Controversial 'gene drive' research sparking ethical debate' *Daily Mail* (London 6 September 2016) http://www.dailymail.co.uk/wires/afp/article-3775353/Controversial-DNA-research-sparks-ethical-debate.html Last accessed 10th May 2017.

[14] Ibid Esvelt.

[15] Carter T Atkinson and Dennis A LaPointe, 'Introduced Avian Diseases, Climate Change and the Future of Hawaiian Honey Creepers' (2009) Journal of Avian Medicine and Surgery 53.

[16] John Min and Others, 'Harnessing Gene Drive' (2018) Journal of Responsible Innovation 40, 47.

[17] Ibid 48.

3. Possible Adverse Consequences of Gene Drive Technologies

Whilst gene drive technologies present heretofore unprecedented opportunities – such as the global eradication of malaria – as suggested earlier, they do not come without equally great risks. This section maps out the adverse consequences of gene drive technologies that have been identified across the range of literature. In later Chapters, I turn to a discussion of adverse effects that have not been identified in discussions surrounding gene drive technologies but, for now, the discussion here focuses on those possible adverse effects agreed on by the scientific community. Before I begin however, one note of caution. In much of the material that contemplates the regulation of gene drive technologies, discussion of the technology's benefits takes place in concrete terms. That gene drive technologies might be a means of eliminating malaria is allegedly certain. Beyond the confidence and certainty with which claims as to the benefits of the technology are made, however, we are able to understand, in a very real way, what the elimination of malaria means.

In that way, the benefits that gene drive technologies might bring are easily articulated and easily understood. The same is not true in discussions of the risks or burdens that gene drive technologies present. Instead, discussions about the risks and burdens are conducted in both abstract and hypothetical terms. They are difficult to articulate and even harder to understand. These difficulties are in part a function of the fact that current understandings of the risk implications of gene drive technologies are relatively meagre. It does, however, have the effect of minimizing the perceived relevance of the risks when they are presented alongside the concrete benefits.

3.1 Off-target Edits

An off-target edit is an unintended genome modification. Off-target edits occur when the tools used for gene editing bind to and alter a non-target sequence of DNA. This can happen when both the target and non-target sequence share a sequence of DNA base pairs. For example, the genetic modification might seek to remove a gene with a base pair sequence:

ATCGATTGAGCTCTAGC. However, this sequence might occur at several other sites throughout the organism's genome, as part of a longer sequence coding for another gene. The gene editing machinery does not distinguish between the two lengths of sequence and will therefore bind to both, cutting them out and leaving a cut in the DNA strand to be repaired by the organism's own DNA repair mechanisms. Alternatively, off-target edits take place when there is a partial mismatch between the sequence that the editing machinery is programmed to edit and the sequence that it actually binds to. As such, off-target effects can cause unintended genetic mutations across the genome of the edited organism.

As with all genetic mutations, the effects of off-target edits can vary. For instance, the off-target edit might occur in a non-functional region of the DNA sequence, thus having no effect on the edited organism at all. Alternatively, off-target edits might affect the functionality of the protein that the mutated base-pair sequence codes for – resulting either in a protein that does not work as it should, or a protein that does not work at all.[18]

The possible consequences of off-target edits using CRISPR gene-editing techniques hit the headlines toward the end of 2018, when Chinese Scientist He Jiankui announced that he had used CRISPR-based techniques to edit the genomes of twin babies, in an attempt to confer HIV resistance on the pair.[19] Following Jiankui's announcement, the study received considerable scrutiny from scientific colleagues who expressed considerable concern about the health consequences that off-target effects might bear for the twins.[20] Several scientists have commented on the possibility that the edits that Jiankui made were unlikely to have conferred HIV resistance at all whilst simultaneously reducing the life expectancy of the twins.[21] Amongst the concerns noted

[18] For a helpful explainer on the possible effect of genetic mutations see: US Library of Medicine, Genetics Home Reference, 'What Genetic Mutations Are Possible?' https://ghr.nlm.nih.gov/primer/mutationsanddisorders/possiblemutations Last accessed 4th September 2019.
[19] David Cyranoski & Heidi Ledford, 'Genome-edited baby claim provokes international outcry' (*Nature News*, 26 November 2018) https://www.nature.com/articles/d41586-018-07545-0 Last accessed 4th September 2019.
[20] Katrina Zimmer, 'CRISPR Scientists Slam Methods Used on Gene-Edited Babies' (*The Scientist,* 4 December 2018) https://www.the-scientist.com/news-opinion/crispr-scientists-slam-methods-used-on-gene-edited-babies--65167 Last accessed 4th September 2019.
[21] Sara Reardon, 'Gene edits to 'CRISPR babies' might have shortened their life expectancy' (*Nature News*, 4 June 2019) https://www.nature.com/articles/d41586-019-01739-w Last accessed 4th September 2019.

by the scientific community was the possibility that off-target edits had increased the twins' risk of cancer[22] and that incidental effects of the edits altered the cognitive abilities of the twins.[23]

Whilst the above provides a discussion of the consequences of off-target edits as a way into understanding the potentially serious effects of unintended mutations, what are the implications of off-target edits for gene drive technologies? At present, understandings about what off-target edits might occur and how they could manifest are scarce. However, as Webber and others note, concerns about off-target edits are even more acute in the gene drive context than the therapeutic context discussed above.[24] This is because the CRISPR-based gene editing machinery remains *in situ* across generations and therefore off-target edits are replicated and increase in frequency, therefore amplifying any harms that do arise as a consequence of off-target edits.

At best, the occurrence of functional off-target effects might render the gene drive ineffective, thus failing to provide the promised benefits. At worst, off-target edits might cause unanticipated ecological disturbances – the drastic consequences of which are described below.

3.2 Horizontal Gene Transfer

Whilst vertical gene transfer refers to the movement of genes from a parent organism to its offspring, horizontal gene transfer refers to the movement of genes between populations of distinct species. Concerns regarding horizontal gene transfer describe the potential for the genetic information coding for a gene drive moving from the target species to a non-target species. For example, horizontal gene transfer could cause a population suppression drive for *Anopheles gambiae* to spread into another species. The non-target species could be another species of mosquito, but it could be another species entirely, such as moth, bee or fruit fly.

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[22] Jon Cohen, 'Did CRISPR help – or harm – the first ever gene edited babies?' (*ScienceMag,* 1 August 2019) https://www.sciencemag.org/news/2019/08/did-crispr-help-or-harm-first-ever-gene-edited-babies Last accessed 4th September 2019.

[23] Antonio Regalado, 'China's CRISPR twins might have had their brains inadvertently enhanced' (*MIT Technology* Review, February 21st 2019) https://www.technologyreview.com/s/612997/the-crispr-twins-had-their-brains-altered/ Last Accessed 4th September 2019.

[24] Bruce Webber et al, 'Is CRISPR-based Gene Drive a Biocontrol Silver Bullet or a Global Conservation Threat?' (2017) PNAS 10565, 10566.

As the National Academies of Science, Engineering and Mathematics report (hereafter 'NASEM Report') suggests, current understandings of what causes horizontal gene transfer, when it might happen and whether it is more likely to happen between certain species, are limited.[25] As such, it is difficult to predict what the implications of horizontal gene transfer might be. However, existing evidence demonstrates that horizontal gene transfer can take place across biological domains and, as such, we can observe genes moving from bacteria to eukaryotes (non-single celled organisms) and *vice versa*.[26] Furthermore, whilst horizontal gene transfer would not alter populations at great speed, the population changes that it can effect are profound.[27]

The implications of horizontal gene transfer for the use of gene drive technologies are little understood by the technical experts offering up predictions about the ill-effects of gene drive technologies. This is because whilst the molecular biologists describing the risks of gene drive technologies explain the molecular mechanism through which horizontal gene transfer occurs, it is ecologists and population biologist that are best placed to predict what the implications of horizontal gene transfer might be in local ecosystems.

In theory, if a population suppression drive were to move into a non-target species, we might see suppression of the non-target species. Whether this sort of horizontal gene transfer proves problematic depends on the identity of the non-target species. For instance, if a suppression drive were to move into a species of pollinating insects and crash the population pollinators, the effects scarcely need rehearsing. Furthermore, whilst eradicating the target species might be non-problematic from an ecological perspective, the unintended eradication of the non-target species by horizontal gene transfer could prove less ecologically benign. The effects of interference with ecological systems can be varied and will be discussed below.

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[25] National Academies of Science, Engineering and Mathematics Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct, 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' (Washington: National Academies Press) 144. Hereafter, ("NASEM").

[26] E Hilario and J P Gogarten, 'Horizontal transfer of ATPase genes—the Tree of Life becomes the Net of Life' (1993) Biosystems 111.

[27] J P Gogarten and J P Townsend, 'Horizontal gene transfer, genome innovation and evolution' (2005) Nature Review of Microbiology 679.

3.3 Gene Flow

Gene flow refers to the flow of genes from one population of a target species to another population of the same species. This most often happens when individuals of a species move from one population to another. This movement might be caused by means of human interference, for instance humans moving organisms from one region to another, where the displaced organisms then find mates in their new home. Alternatively, individuals might move into new populations in response to changes to their habitat – whether forced out by forest fires, or carried away by flash flooding.[28] Less drastic changes to their habitat such as insufficient breeding sites or inadequate food resources might also cause individuals to move to new populations, taking their genetic information with them.[29]

Given the self-sustaining, self-proliferating nature of gene drive technologies, gene flow will occur at a high rate when gene drive organisms are released, spreading the gene drive genotype through wild-type populations. This might not always be a bad thing – in the case of a population suppression drive designed to tackle malaria, spreading the genotype that interrupts female fertility to other populations will ensure the widespread removal of the *Anopheles* vector. In this way, gene flow causing the suppression or eradication of a number of populations is desirable insofar as it proves a quick, effective and efficient way of controlling vector populations. The high rate of gene flow that gene drive technologies can cause might even be characterized as *the* defining virtue of the technology because oftentimes high rates of gene flow is precisely what we are trying to achieve.

As such, whether gene flow is considered an adverse consequence of gene drive technologies can only be assessed on a case-by-case basis, taking into account the purpose for which the drive is designed. If a gene drive is intended only to affect a single target population of a species, and

[28] For just one example of gene flow following habitat change see: T C McElroy et al, 'Temporal Population Genetic Structure of Eastern Mosquitofish in a Dynamic Aquatic Landscape' (2011) Journal of Heredity 678.
[29] J Clobert et al, 'Causes, Mechanisms and Consequences of Dispersal' in I Hanski and O E Gaggiotti (eds) *Ecology, Genetics and Evolution of Metapopulations* (Boston: Elsevier 2004).

the spread of the drive mechanism into non-target populations would be undesirable, gene flow presents a real challenge to both the design of the drive and how it ought to be regulated.

Furthermore, understanding the effects of gene flow has important implications for understanding the spatial spread and dynamics of a gene drive and how off-target effects might be spread throughout a population. As the NASEM Report suggests, at present the models that exist for understanding the effect of releasing gene drive organisms within wild-type populations have significant empirical shortcomings and thus if in future were are to be able to predict the effects of gene drive technologies with any confidence, significant research within this domain ought to be pursued.[30]

3.4 Evolutionary Interruption

Evolutionary biology also provides some insights into what the adverse consequences of a gene drive release could look like. In the first instance, and as the NASEM Report notes, many interactions between species are not just ecological process, but the result of evolution.[31] For example, the report highlights pathogen-hosts systems, such as the one observed between *Anopheles gambiae* and *Plasmodium falciparum.*[32] In these pathogen-host systems, the features of both species develop in co-evolution with one and other. Due to the evolutionary links between the two species, the removal or alteration of one species can have drastic effects on the other. These drastic effects can manifest as ecological disturbances as discussed below, or the development of genetic alteration or resistance in the co-evolved species.[33] In the context of a population alteration drive conferring pathogen resistance on vectors this might result in pathogens evolving to overcome resistance or being carried by other species. This in turn, could result in more virulent pathogens, or a greater abundance of the pathogens, causing either more aggressive strains of the diseases that they cause, or higher rates of disease within the population.

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[30] NASEM (n25) 39.
[31] Ibid 41; Kerr *et a*l, 'Myxoma Virus and the Leporipoxviruses: An Evolutionary Paradigm' (2015) Viruses 1020.
[32] M A Duffy and S R Hall, 'Selective Predation and Rapid Evolution can Jointly Dampen Effects of Virulent Parasites on Daphina Populations' (2008) Am Nat 499.
[33] NASEM (n22) 40.

3.5 Ecological Disturbances

Both population suppression drives and population alteration drives are likely to alter the ecology of the areas within which they are released – and given the gene flow phenomena cited above, far beyond. Ecological systems are complex, replete with non-linear relationships and dynamic feedback loops.[34] Species are connected within ecological communities through both direct and indirect connections. For example, species might exist in a direct, predator-prey relationship with one and other, much like cats and mice, lions and gazelle. Alternatively, species might share indirect relationships with each other, competing for the same resources. For example, squirrels and woodpeckers compete for the same nesting spots and the lions hunting gazelle compete against cheetahs for their share of the quarry.

All of these various intra-specific relationships exist in relation to one another, creating almost innumerable feedback loops and therefore a system of high complexity, making accurate predictions about any interferences difficult to obtain.[35] In this respect, and as the NASEM Report notes, there exists very considerable epistemic uncertainty about the ecological consequences of gene drive technologies, and, at present, there exists little consensus on how these knowledge gaps might be closed.[36]

What then are some of the potential implications of ecological disturbances caused by gene drive technologies? In the first instance, there exist concerns that instead of reducing disease burden, gene drive technologies could, by disturbing the equilibria in complex ecological systems, increase disease burden. In their 2005 report, Snow *et al* note the risk that genetic alteration of populations might create new or more vigorous pests or pathogens.[37] In the context of population suppression drives, this could occur if, for example, eradicating the malaria vector *Anopheles Gambiae* caused a boom in the population of another vector species by removing its key competitor.

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[34] Ibid.
[35] S J Leroux and M Loreau, 'Consumer-mediated recycling and cascading trophic interactions' (2010) Ecology 262.
[36] NASEM (n25) 42.
[37] A A Snow and D A Andow et al, 'Genetically Engineered Organisms and the Environment: Current Status and Recommendations' (2005) Ecological Applications 377, 378.

On the other hand, in the case of population replacement drives, we worry about the unintended effects of replacing a particular genotype within a population. For example, could conferring malaria resistance on *Anopheles gambiae* make them more efficient dengue vectors?

Despite the promising public health applications of gene drive technologies, they are not without significant risks. The range of adverse consequences discussed above demonstrates the ways in which gene drive technologies have the propensity to cause great harm – by increasing disease burden or causing irreversible ecological disturbances with severe consequences for the human communities implicated. The adverse consequences tabled above reflect the totality of discussions about the possible undesirable implications of gene drive technologies. All of the risks or adverse consequences under discussion are the product of scientific findings and technical expertise. No thought is given to the way these adverse outcomes might interact with one and other, and little effort is taken to translate these technical understandings into the social, political or cultural implications that they might have, and in turn the harms that they might occasion. That is not to say that these understandings are unimportant or irrelevant, because they are not. They are vital to building an understanding of the technology that reflects its reality, but they only render half of the rich and complex picture.

4. Developments in Gene Drive Technology: Research & Regulation

One of the contentions that this thesis makes is that, at present, there is no framework adequate for the regulation of gene drive technologies. Despite this, however, progress in the lab pushes us ever closer to release in the field and therefore the realisation of the wide range of both benefits and burdens. This section records the progress that has been made in gene drive research, looking at both developments in the lab and the ways in which they inform developments in the field. In doing so, I illustrate the choices that are being made in the regulatory void and which knowledge claims are being privileged in the thinking that takes place around the use and regulation of gene drive technologies.

Once I have outlined the ways in which research has developed, I then move to consider what has been said from a regulatory perspective. This involves reviewing the publications of a number of governmental and non-governmental organisations, with an eye on two things in particular. The first is the way in which the reports conceive of the technology as a regulatory object, and the second is the way in which these conceptions inform the views espoused *viz a viz* the regulation of gene drive technologies.

This analysis serves several purposes. Firstly, it functions to provide a helpful, up to date conspectus of current thinking around the regulation of gene drive technologies. Given the scant literature surrounding their regulation, the implications of these publications have yet to have been considered along-side each other. Secondly, this analysis develops a picture of the ways in which gene drive technologies are being thought about from a regulatory perspective, again providing an illustration of the values (or more commonly, lack thereof) that are implicated and the knowledge claims that are allowed to take precedence. In this way, I argue that, at present, discussions surrounding gene drive technologies and their regulation can be characterized by the hegemony of technical expertise.

4.1. Research Developments

As suggested above, gene drive technologies in and of themselves are not new. In the 1920's Sergey Gershenson observed the existence of selfish genetic elements.[38] In the early 2000's, Austin Burt pursued considerable research into how this selfish gene might be used for the control of insect populations.[39] However, the real turning point came with the development of CRIPSR-based gene editing techniques by Jennifer Doudna and others in 2012.[40] Compared to their predecessors, CRISPR-based gene editing techniques were cheaper, more precise, more effective and took less time to use. As such, gene drive researchers moved away from using conventional gene editing

[38] Sergey *Gershenson, 'A New Sex-Ratio Abnormality in DROSOPHILA OBSCURA' (1928) Genetics 488.*
[36] A Burt and R Trivers, Genes in Conflict: The Biology of Selfish Genetic Elements (Harvard University Press, 2009).
[40] J Doudna et al, 'A Programmable dual-RNA-guided DNA endonuclease in Adaptive Bacterial Immunity' (2012) Science 816.

techniques in order to build their gene drive systems and toward CRIPSR-based techniques.[41] Gene drives were first developed in yeast strains[42] and soon after, unintentionally, one research team built a gene drive in *Drosophila melanogaster* or the common fruit fly.[43]

In November 2015, Gantz and others released a proof of principle for a population alteration drive conferring resistance to a malaria vector of the mosquito species *Anopheles stephensi*.[44] One month later, Hammond and others published their paper providing a proof of principle for a population suppression drive for the malaria vector *Anopheles gambiae*.[45]

Following the publication of papers by both Gantz and others and Hammond and others, interest in CRISPR-based gene drives grew. Not only were research teams interested in considering new and novel applications for the technology, research was focused on how gene drive technologies and research into them might be made safer. As such, Kevin Esvelt's team in particular worked on developing gene drive technologies that could be limited in terms of both their temporal and spatial spread. Esvelt's team published a number of papers detailing what they call 'Daisy-chain Drives'.[46] Esvelt's research suggests the possibility of building gene drive systems that will 'drop out' of populations overtime, thus allowing at least some control of the spread of the technology.

Since the development of gene drives in various insects, scientists have set their sights on larger organisms.[47] Kevin Esvelt's team are working on population alteration gene drives designed to confer immunity to tick-born disease on mice.[48] Other scientists have developed gene drive

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[41] K Esvelt et al, 'Concerning RNA-guided Gene Drives for the Alteration of Wild Populations' (2014) eLife e03401i
[42] L Cong et al,'Multiplex Genome Engineering Using CRISPR/Cas Systems' (2013) 819.
[43] SJ Gratz *et al,* 'Genome engineering of Drosophila with the CRISPR RNA-guided Cas9 nuclease' (2013) Genetics 1029.
[44] Gantz *et al*, 'Highly Efficient Cas9-mediated Gene Drive for Population Modification of the Malaria Vector Anopheles stephensi' (2015) PNAS e6736.
[45] Hammond *et al*, 'A CRISPR-Cas9 Gene Drive System Targeting Female Reproduction in the Malaria Mosquito Vector *Anopheles gambiae'* (2016) Nature Biotechnology 78.
[46] Esvelt *et al*, 'Daisy-chain Gene Drives for the Alteration of Local Populations' (2019) Proceedings of the National Academy of Science 8275.
[47] Bruce R Conklin, 'On the Road to a Gene Drive in Mammals' (2019) (*Nature News,* 23 January 2019) https://www.nature.com/articles/d41586-019-00185-y#ref-CR5 Last accessed 5th September 2019.
[48] 'Preventing tick-borne disease by permanently immunizing mice' https://www.media.mit.edu/projects/preventing-tick-borne-disease-by-permanently-immunizing-mice/overview/ Last accessed 25th September 2019.

systems in mice, designed to alter the coat-colour of the population.[49] In Edinburgh one research team is seeking to develop gene drives causing infertility in both mice and rats as a novel means of pest control.[50] In California, a team of scientists funded by the California Cherry board have developed a gene drive to eradicate the spotted wing drosophila, the scourge of many a fruit farmer.[51] This latter drive demonstrates that the road towards commercial applications of gene drive technologies has already been paved, the consequence of which are picked up in Chapter Seven in the context of exploitation.

Reviewing the range of gene drive research currently being pursued, it becomes clear that in the absence of regulation that articulates a position on the acceptable and legitimate uses of gene drive technologies, research pushes on in all directions. The scientific community has taken no position on what benefits might justify the considerable burdens gene drive technologies might bring with them and have instead pursued all conceivable applications of the technology, from public health to commercial agriculture.

4.2. Developments Towards the Release of Gene Drive Organisms

Not only have there been significant advances in the technology, but some progress has been made towards its deployment in the field too. Target Malaria is a not-for-profit research consortium funded primarily by the Bill and Melinda Gates Foundation.[52] The research consortium is comprised of scientists, stakeholder engagement experts, risk assessment specialists, project managers and communications professionals.[53] Whilst most of the basic research carried out takes place in University research programmes in the United Kingdom and the United States, Target

[49] Grunwald et al, 'Super-Mendelian Inheritance Mediated by CRISPR-Cas9 in the Female Mouse Germline' (2019) Nature 105.
[50] The Roslin Institute, 'Gene Experts Set to Tackle Pest Control' (*Roslin Institute*, 6 December 2017) https://www.ed.ac.uk/roslin/news-events/archive/2017/gene-experts-tackle-pest-control Last accessed 5th September 2019.
[51] Antonio Regaldo, 'Farmers Seek to Deploy Powerful Gene Drive' (*MIT Technology Review*, 12 December 2017) https://www.technologyreview.com/s/609619/farmers-seek-to-deploy-powerful-gene-drive/ Last accessed 8th September 2019.
[52] --, 'Who We Are' (Target Malaria, August 2019) https://targetmalaria.org/WhoWeAre Last accessed 12th September 2019.
[53] Ibid.

Malaria has active projects running in Mali, Burkina Faso, Uganda and Ghana.[54] Target Malaria has ear marked Burkina Faso for the first release of gene drive technologies as early as 2023.[55]

At present, Target Malaria has built insectaries in Mali, Burkina Faso and Uganda. In August 2018, Target Malaria received authorization for the release of 10,000 sterile, genetically modified mosquitos from the National Biosafety Agency of Burkina Faso.[56] This release took place in July 2019.[57]

Whilst Target Malaria has a strong track record of investing in co-development of the technologies and pursuing responsible 'stake holder engagement', that plans for the release of gene drive organisms are forging ahead in countries with unsuitable regulation and significant infrastructural inadequacies presents cause for serious concern.[58] In both Mali and Burkina Faso, the laws currently governing the release of gene drive technologies are modelled on the European Union regime for the Regulation of GMO's, the inadequacy of which is discussed in Chapter Four.

In February 2019, a Target Malaria funded research team began caged trials on gene drive modified *Anopheles gambiae* in Terni, Italy.[59] This set of experiments was designed to gather more data about how these organisms might behave in organisms released into the wild, and as such the conditions into which the modified organisms were released were designed to mimic natural

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[54] Ibid.

[55] Dylan Matthews, 'Gene Drives Could End Malaria. And they Just Escaped a UN Ban' (*Vox*, 7 December 2018) https://www.vox.com/future-perfect/2018/12/7/18126123/gene-drive-malaria-convention-biological-diversity Last accessed 6th September 2019.

[56] Arrete No.2018-456/MESRSI/SG/ANB portant authorisation de dissemination controlee de moustiques males sterlies genetiguement modifies dans le village de Bana ou de Souroukoudingan http://bf.biosafetyclearinghouse.net/autorisation%20d%27une%20diss%C3%A9mination%20contr%C3%B4l%C3%A9e%20de%20moustiques%20gm%20dans%20le%20village%20de%20bana%20ou%20de%20souroukoudingan.pdf Last accessed 6th September 2019.

[57] Abdoulaye Diabate, 'Target Malaria Proceeded with small-scale release of genetically modified sterile mosquitos in Bana, a village in Burkina Faso' (*Target Malaria,* 1st July 2019) https://targetmalaria.org/target-malaria-proceeded-with-a-small-scale-release-of-genetically-modified-sterile-male-mosquitoes-in-bana-a-village-in-burkina-faso/ Last accessed 6th September 2019.

[58] Sarah Hartley et al, 'Knowledge Engagement in Gene Drive Research for Malaria Control' (2019) PLoS Neglected Tropical Disease e0007233.

[59] Rob Stein, 'Scientists Release Controversial Genetically Modified Mosquitoes In High-Security Lab' (*NPR*, 20 February 201) https://www.npr.org/sections/goatsandsoda/2019/02/20/693735499/scientists-release-controversial-genetically-modified-mosquitoes-in-high-securit?t=1567762912883 Last accessed 6th September 2019.

environments. Given Target Malaria's plans for their first open release in 2023, the test in Terni is likely to the first of many experiments in progressively less confined and secure conditions.

As such, despite the lack of adequate regulation, beyond the laboratory gene drive technologies push closer and closer to release into the communities within which the benefits and the burdens of the technology will be distributed.

4.3. Funding and Investment Developments

In 2017, the United States' Military became the largest single funder of gene drive research.[60] The establishment of the Safe Genes Programme by the Defence Advanced Research Projects Agency (DARPA) signals a significant commitment to countering concerns regarding the dual use nature of gene drive technologies.[61] The programme funds research into advanced prophylactics against gene editing technologies, as well as research into the remediation and reversal of existing techniques.

The central role of the US military in funding gene drive research has not been without criticism and concern. As Brossard and others have noted, a range of voices has expressed concern that military involvement might lead to research into the weaponization of gene drive technologies.[62] Furthermore, Todd Kuiken, a Senior Research Associate attached to a laboratory conducting gene drive research, wrote an online blog expressing concern regarding the ways in which this funding would affect future research directions.[63]

The progress discussed above demonstrates that, despite the absence of adequate regulation, the development of gene drive technologies pushes on unabated, treating some of the most crucial questions that we might have about their use as if settled, or unimportant. The scientific

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[60] Arthur Neslen, 'US Miltary Agency Invests $100m in Genetic Extinction Technologies' (*The Guardian*, 4 December 2017) https://www.theguardian.com/science/2017/dec/04/us-military-agency-invests-100m-in-genetic-extinction-technologies Last accessed 6th September 2019.

[61] Renee Wegrzyn, 'Safe Genes' (*DARPA*, December 2017) https://www.darpa.mil/program/safe-genes Last accessed 6th September 2019.

[62] Dominque Brossard et al, 'Promises and Perils of Gene Drives: Navigating the Communication of Complex, Post-Normal Science' (2019) Proceedings of the National Academy of Sciences 7692, 7693.

[63] Todd Kuiken, 'DARPA's Synthetic Biology Initiatives Could Militarize the Environment' (*Slate*, 3 May 2017) https://slate.com/technology/2017/05/what-happens-if-darpa-uses-synthetic-biology-to-manipulate-mother-nature.html Last Accessed 6th September.

community is concerned with what gene drive technologies can do, and what gene drives they might be able to develop, and so they push on, answering only those questions. All the while, those questions surrounding the burdens that gene drive might confer, and upon who those burdens might be heaped, go unasked and unanswered. There is little pause to ask whether these are world states that we ought to bring about and where the line between laudable and impermissible applications of gene drive technologies might be drawn.

4.4 Policy Papers

Whilst no framework adequate for the regulation of gene drive technologies currently exists, the regulatory position has been the subject of debate amongst regulators and academics. This section describes commentary regarding the regulation of gene drive technologies as it appears in the publications of various different governmental and non-governmental organisations. At the outset it is worth noting that all of the reports find that gene drive technologies fall to be regulated by legislation covering the use of Genetically Modified Organisms in the jurisdictions that they discuss. The reasons for which this is problematic are outlined at length in Chapter Four, but for now it suffices to say that such a view adopts a particular conception of gene drive technologies and their place in the world. The views espoused in these reports deserve careful study as they will, in all likelihood, play a significant role in shaping future regulatory responses.

4.4.1. Report of the National Academies of Science, Engineering & Mathematics

In 2016, the United States National Academy of Science, Engineering and Mathematics published their report, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values* (hereafter 'NASEM Report').[64] This Report presented the first, and to date only, comprehensive review of gene drive technologies with regard to how they might be used and the benefits and burdens that they might distribute. The Report notes that the way the technology

[64] National Academies of Science, Engineering and Mathematics Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct, 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' (Washington: National Academies Press).

intentionally spreads a genetic trait throughout a population, and the fact that the spread is potentially irreversible, mark the technology out as novel and therefore worthy of special consideration. The Report also reviews the current state of knowledge *viz a viz* understandings of the environmental and ecological consequences of the technology. Ultimately, the Report concludes:

> There is insufficient evidence available at this time to support the release of gene-drive modified organisms into the environment. However, the potential benefits of gene drives for basic and applied research are significant and justify proceeding with laboratory research and highly controlled field trials.[65]

The Report makes a range of recommendations throughout, calling, in particular, for public engagement in decision making,[66] the avoidance of a 'one size fits all' approach to regulatory decision making[67] and the international harmonization of governance.[68] The Report also identifies knowledge gaps in the domains of 'molecular biology, genome editing, population genetics, evolutionary biology and ecology' and recommends significant effort be mounted in order to fill these gaps.[69]

Whilst the Report does provide the most comprehensive consideration of gene drive technologies and their implications, the treatment of many of the issues is somewhat superficial. In particular, it presents an understanding of the technology and its place in the world that is problematic in a range of ways. In the first instance, the recommendation that human values be taken into account is little more than the suggestion that we weigh the potential harms and benefits that the technology might provide for human communities. As such the Report presupposes consensus with regard to what constitutes relevant harm and benefit, and to whom they might accrue. In this way, the Report fails to conceive of gene drive technologies as presenting a novel question in respect of harm and benefit and how they might be distributed or shared. Furthermore, the report assumes that each benefit and harm might then be totted up on a utilitarian balance

[65] Ibid 10.
[66] Ibid
[67] Ibid
[68] Ibid
[69] Ibid 42.

sheet, the bottom line of which will tell us what we ought to do. As this thesis goes on to suggest, one of the most challenging aspects of trying to regulate gene drive technologies is accurately identifying the harms and benefits that the regulation should seek to avoid or control and furthermore, who it is that regulation should be concerned to regulate and who it is regulation should be concerned to protect. For the most part, the Report treats these issues as settled.

Secondly, as will be expanded upon further in Chapter Four, the neat boundary that the Report draws between 'environmental release' – which it does not support, and 'field trials' which it does support is, given the nature of the technology, largely illusory. This is problematic as, if the distinction between environmental release and experimental release is illusory, the representations of the technology given in the Report lack any fidelity to the technology as a regulatory object.

Finally, the knowledge gaps the Report identifies pertain only to a narrow range of knowledge claims that regulatory decision making might take into account. That is, the Report only advocates for the development of further technical expertise – specifically in those domains outlined above. I do not mean to suggest here that development in those domains is not vital to robust decision making around gene drive technologies. Instead, my concern is that whilst such developments are indeed necessary, they alone are not sufficient to guarantee good decision making in the regulatory context. As I contend in Chapter Three, there exists a range of knowledge claims beyond technical expertise that are vital to identifying the harms and benefits gene drive technologies present us with, as well as identifying persons affected by the technologies.

4.4.2 Report of the Dutch Government

In September 2016, the Institute for Public Health and the Environment, a body of the Ministry of Health, Welfare and Sport for the Dutch Government, published *Gene Drives: Policy Report.*[70] This report concludes that, broadly speaking, the current European Union framework for the Regulation of GMOs provides a suitable basis for the regulation of gene drive technologies.[71] The

[70] J Westra et al, 'Gene Drives: Policy Report' (Institute for Public Health and the Environment, 2016) (The Netherlands) https://www.rivm.nl/bibliotheek/rapporten/2016-0023.pdf Last accessed 5th September 2019.
[71] Ibid 26.

reasons for which this is problematic are drawn out in some detail in Chapter Four, but suffice to say here that such a scheme of regulation cannot anticipate and control the benefits and burdens of gene drive technologies. That the use of gene drive technologies might raise important ethical implications is dealt with in one paragraph under the heading 'Other Points of Concern' at the end of the report.[72] The report only notes that ethical issues might exist, it takes no position on what they might look like, or how they ought to be taken account of in the regulatory context. The report does however, express concerns that the current risk assessment methodologies for GMOs might be inadequate for assessing the risks associated with gene drive technologies.[73] In part, this is because, much like the NASEM Report, this report suggests that the self-proliferating and potentially irreversible nature of the technology presents novel technical challenges that require further research to overcome. In this way then, questions about how gene drive technologies ought to be regulated can be resolved through analytical methodologies rendering technical solutions to the technical challenges that gene drive technologies pose.

4.4.3 Report of the Royal Society

In November 2018, the Royal Society published a report entitled, *Gene Drive Research: Why It Matters.*[74] This report was published in advance of the Convention on Biological Diversity's second scheduled debate on a moratorium of gene drive research.[75] The report explicitly denounces the possibility of a moratorium, noting that whilst, at present, the risks and benefits associated with gene drive technologies are uncertain and difficult to characterise, more research ought to be undertaken in order to overcome these challenges.[76] In this respect, the report takes the view that the development of further technical expertise in the research context ought to be sufficient to

[72] Ibid 29.
[73] Ibid 26.
[74] Royal Society, 'Gene Drive Research: Why it Matters' https://royalsociety.org/-/media/policy/Publications/2018/08-11-18-gene-drive-statement.pdf Last accessed 5th September 2019.

[75] United Nations, Convention on Biological Diversity (1992); See: Ewen Calloway, 'UN treaty agrees to limit gene drives but rejects a moratorium' (Nature News 28 November 2018) https://www.nature.com/articles/d41586-018-07600-w Last accessed 22nd September 2019.
[76] Royal Society (n74) 3.

enable accurate characterisation of the risks and benefits of gene drive technologies. However, the report does note that any future use of gene drive technologies ought to be preceded by public debate about the desirability of their use.[77] In the broader context of the report, this suggestion appears to be motivated by concerns for public opinion regarding the legitimacy of any given gene drive release, rather than the idea that public involvement might play a role in the regulatory process by aiding the way that we go about characterising the risks and benefits associated with gene drive technologies.

4.4.4 Report of the Australian Academy of Science

In May 2017, the Australian Academy of Science delivered a short, 12-page report entitled, *Synthetic Gene Drives in Australia: Implications of Emerging Technologies*.[78] This report considers what uses gene drive technologies might be put to in Australia – particularly focusing on the species elimination capabilities of the technology, *viz a viz* Australia's historical and current problems with invasive species.[79] Like the other reports discussed above, this report focuses on the need to develop further technical expertise in order to overcome issues of uncertainty in respect of both the risks and the benefits of the technology.[80] Interestingly, this report is the only one to raise the societal and ethical implications of commercializing gene drive technologies.[81] These issues are raised again in depth, in Chapter Seven of this thesis. The rest of the discussion surrounding the societal implications of gene drive technologies raises concerns about the technology being subject to the same public derision that conventional GMOs faced and, therefore, like the Royal Society report, takes a rather instrumental view of the role of public participation in the regulation of new technologies.

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[77] Ibid 7.
[78] The Australian Academy of Sciences, 'Discussion Paper: Synthetic Gene Drives in Australia: Implications of Emerging Technologies' https://www.science.org.au/files/userfiles/support/documents/gene-drives-discussion-paper-june2017.pdf Last accessed 5th September 2019.
[79] Ibid 5.
[80] Ibid.
[81] Ibid 8.

4.4.5 Report of the African Union

In 2018, the High-Level African Panel on Emerging Technologies convened by the African Union published a report entitled, *Gene Drives for Malaria Control and Elimination in Africa.*[82] Like this thesis, the report confines it analysis only to malarial applications of gene drive technologies. This report makes recommendations in line with those of the other reports discussed above – advocating for the development of further technical expertise. Further the report calls for regulatory collaboration between Member States of African Union and investment in the infrastructures required for the safe and effective deployment of gene drive technologies.[83]

Perhaps the most interesting aspect of the report is the short but telling paragraph focusing on the gender impact of gene drive technologies.[84] The report suggests that previous malaria control strategies, such as the use of bed nets, have had particular gendered implications. In the first instance, the report notes that bed net strategies have focused on preventing malarial disease in children and pregnant women. As a consequence, the report notes that there has been an inequality in provision for young adults and men.[85] However, the report also notes that women may have 'compromised decision-making roles when it comes to choosing which members of the household should or should not use the available bed nets'.[86] The report goes on to note that:

> Gene drive on the other hand, would not be dependent on individual use or compliance and would instead provide extensive communal benefits regardless of age or gender of individual members of the communities. [87]

In this way the report clearly conceives of gene drive technologies as a technical solution to a technical problem. At various points throughout this thesis I describe the dubious merit in describing gene drive technologies and their implications in these terms. However, as is demonstrated at some length in Chapter Four, considering gene drive technologies as insusceptible

[82] Report of the High Level African Panel on Emerging Technologies, 'Gene Drives for Malaria Control and Elimination in Africa' https://www.nepad.org/publication/gene-drives-malaria-control-and-elimination-africa Last accessed on 5th September 2019.
[83] Ibid.
[84] Ibid 21.
[85] Ibid.
[86]Ibid.
[87] Ibid.

to the whims of human behaviour and culture, as this report does, presents a significant flaw in current thinking surrounding the technology.

What emerges from the reports above is a tendency to speak of gene drive technologies as a technological solution to a technological problem and, furthermore, as any risks or uncertainties as reducible by doing more science. Concerns that gene drive technologies might run, ecologically, amok are quelled by suggestions that scientists might develop spatially or temporally limited systems, not taken as a prompt to consider what world states we ought to bring about. Suggestions that gene drives technologies could cause irreversible harms occasion the offering up of designs for 'reversal drives' rather than consideration of the infrastructures necessary to ameliorate those harms.

4.5 Legislation & Regulation

Discussions of the regulation of gene drive technologies have not been limited to policy reports – some analysis has been offered up in the academic literature too. This section reviews the relatively little that has been written, before offering some concluding remarks on the ways in which gene drive technologies have been understood and represented to date.

4.5.1 Academic Commentary

As quickly as the various proof of principles for gene drive technologies burst on to the scene following the development of CRISPR-based gene editing techniques, so too did a number of academic commentaries on how gene drive research ought to be carried out and how the technology ought to be regulated.

Oye and others published 'Regulating Gene Drives'.[88] Their paper focuses on advocating for the integrated management of environmental and security risks.[89] In that vein, they set out ten conditions under which gene drive technology ought to take place.[90] These include recommending that all gene drives are built in tandem with a reversal drive (i.e., another gene drive designed to

[88] K Oye et al, 'Regulating Gene Drives' (2014) ScienceXpress 7658.
[89] Ibid 2.
[90] Ibid 2.

undo the effects of the first) and prescribing the levels of molecular containment under which research ought to take place. In this respect, Oye and others' article presents an important contribution to thinking around how gene drive research might be made safer but, in doing so, presupposes the answers to vital questions surrounding gene drive research. They treat as settled the assumption that gene drive research for a range of purposes ought to be pursued and instead focus on the nitty gritty of getting the science done. To that end, Oye and others' concerns are less about how gene drive technologies ought to be regulated and more about providing technical solutions to technical problems. They are not asking whether we ought to use gene drive technologies and, if so, for what purposes and under what conditions. Instead, they are concerned to prescribe scientific methodologies.

A year later, Akbari and others published a paper prescribing the containment protocols that ought to be adhered to in order to enhance the safety of gene drive research and avoid the accidental escape or unintentional spread of gene drive technologies.[91] The article outlines multiple confinement strategies, advocating that at least two of the strategies ought to be used at any given time when working with gene drive organisms in the laboratory. Akbari and his twenty-six co-authors comprised a significant number of the scientists working with gene drive technologies at the time that the article was published and thus became a sort of manifesto for responsible gene drive research and an indication of the community's willingness to self-regulate.

However, promoting norms of self-regulation did not stop there. In mid-2016, Kevin Esvelt, one of the most prominent pioneers of gene drive technology wrote an article expressing concern that regulation could not keep up with leaps in science.[92] Esvelt argues:

> Regulation will always be too slow. Science is too vast for researchers to reliably foresee the consequences of their work. The problem was neatly summarized by atom-bomb pioneer Robert Oppenheimer: "When you see something that is technically sweet, you go ahead and do it, and you argue about what to do about it only after you have had your technical success." Some technical

[91] O Akbari et al, 'Safeguarding Gene Drive Experiments in the Laboratory' (2015) Nature Biotechnology 927.
[92] Kevin Esvelt, 'Gene Editing Can Drive Science to Openness' (*Nature World View*, 9 June 2016) https://www.nature.com/news/polopoly_fs/1.20043!/menu/main/topColumns/topLeftColumn/pdf/534153a.pdf Last accessed 5th September 2019.

> successes are not to be pursued. But others are desperately needed. How can we hope to tell the difference when science is done behind closed doors?[93]

Esvelt goes on to suggest that answers to which technical successes ought to be pursued and which ought to be left alone might be easier to divine if scientists were to share information and data with each other more openly and from the very earliest stages of research. In this respect, Esvelt also espouses a vision of self-regulation within which scientists decide not just how to do gene drive research but also whether, from a normative perspective, certain gene drive applications ought to be pursued. The problem that Esvelt diagnoses is not novel – at the intersection between law, science and technology, law's tendency to lag behind is well observed. The remedy is rarely for regulators to throw up their hands and accept defeat, handing responsibility over to industry instead.[94]

Furthermore, at various workshops and symposia, Esvelt has advocated for intellectual property law devices to secure the openness that he seeks.[95] In practice however, Jacob Sherkow has noted that whilst Esvelt's plans to put patent protection to work in regulating gene drive research have some promise, there are significant legal gaps that need to be addressed.[96] Furthermore, even if gaps within the intellectual property regime were bridged, whilst this might provide a starting point for regulating gene drive research, the intellectual property regime cannot adequately regulate the deployment of gene drive technologies.

4.5.2 UN Convention on Biological Diversity

Twice at the Conference of the Parties to the UN Convention on Biological Diversity a moratorium on gene drive research and deployment has been proposed.[97] Both times, the Parties

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[93] Ibid 153.

[94] Responding to the similar condemnations of law espoused by John Perry Barlow, Roger Brownsword offers a full account of what this challenge actually means for law and regulation and the way we ought to go about making it in Chapter 6 of: Roger Brownsword, Rights, *Regulation and the Technological Revolution* (Oxford University Press, 2008).

[95] Antonio Regaldo, 'Stop "Gene Spills" Before They Happen' (*MIT Technology Review*, 20 October 2016) https://www.technologyreview.com/s/602633/stop-gene-spills-before-they-happen/ Last accessed 5th September 2019.

[96] Jacob S Sherkow,'Patent Protection for CRISPR: an ELSI Review' (2017) Journal of Law and the Biosciences 565, 572.

[97] Calloway (n75).

to the Convention rejected the proposal. However, at the second meeting in Egypt in 2018, they adopted a decision, part of which affected research in the use of gene drive technologies.[98] The decision called for a precautionary approach,[99] case by case risk assessment,[100] and that:

> where appropriate, the "prior and informed consent", the "free, prior and informed consent" or "approval and involvement" of potentially affected indigenous peoples and local communities is sought or obtained, where applicable in accordance with national circumstances and legislation.[101]

In respect of the first two recommendations, their content mirrors regulatory requirements laid down in the EU GMO Framework, discussed later in Chapter Four. Whilst requiring consent ought to be a welcome innovation, the vagueness of the terms in which it is drafted is problematic. In the short excerpt quoted above, the recommendation calls for 'prior and informed consent', 'free, prior and informed consent' or 'approval and involvement' – three qualitatively different standards of consent. As such, little can be gleamed with respect to what might be required to discharge such an obligation, or, indeed, precisely what that obligation consists of. There is quite some distance between 'free, prior and informed consent' and mere 'approval and involvement'. Furthermore, the recommendation leaves it open to the Parties to determine when such consultation might be considered appropriate, leaving a broad margin of discretion in the performance or non-performance this obligation. Following the Conference of the Parties, Target Malaria's Director of Stakeholder Engagement, commenting on the effect of the recommendation stated, 'For our work, it won't change anything'.[102] Chapter Seven discusses at some length the role of consent in gene drive research but, for now, it suffices to say that the recommendation and industry response paints a picture within which researchers are allowed to decide the extent of their obligations *viz a viz* consent.

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[98] United Nations Convention on Biological Diversity, *Decision Adopted by the Conference of the Parties to the Convention on Biological Diversity: 14/19 Synthetic Biology* CBD/COP/DEC/14/19 30th November 2018.
[99] CBD/COP/DEC/14/19, 11(a)
[100] CBD/COP/DEC/14/19 11(b)
[101] CBD/COP/DEC/14/19 11(c)
[102] Calloway (n75).

As such, whilst some have argued that the Decision of the Conference of the Parties demonstrates a restrictive turn in the regulation of gene drive technologies, in practice it moves little beyond the current and inadequate regulation of gene drive technologies through existing GMO regimes. In part this is due to the vague and ambiguous drafting of the recommendations themselves.

5. Conclusion

What emerges from the discussions charted above is an understanding of gene drive technologies constructed almost exclusively through scientific findings and technical expertise. Discussions of the adverse effects of gene drive technologies are communicated through technical accounts of the molecular mechanisms by which they come about. The scope of the enquiry is rarely extended to ask what the implications of these molecular mechanisms might be for the surrounding communities. Efforts are directed at finding lab-based solutions to potentially global problems. Repeatedly, commentators claim that the perils presented by gene drive technologies might be nixed by progress in the laboratory and further technical innovation. In this way, gene drive technologies are conceived of as a technological solution to a technological problem, with any challenges that the technology presents treated as resolvable by technological means too.

Conceiving of gene drive technologies in an almost exclusively technical manner forestalls any engagement with different expertise that might ask a different yet equally vital range of questions that better our understanding of the technology and our ability to respond to and regulate it. Little thought is given to the social, political or cultural characteristics of the societies within which gene drive technologies might be released or the ethical qualities of such a course of action. Whilst some of the reports and even some of the scientists involved in gene drive research have called for such considerations to be made, no effort has been made to fill these gaps and research marches on regardless.

Whilst some of the reports referred to above do pause to consider the ethics of developing gene drive technologies, most of those discussions reflect instrumentalist conceptions of the role

of public opinion in regulating new technologies. That is to say that those voices calling for a focus on community engagement treat it as a prerequisite to legitimating the uses they strive to put the technologies to, rather than as an opportunity to enrich our understandings of the technology or make determinations about its ethical quality. To that end, most of the discussion labelled 'ethical' in the reports above reflects on the implications that broad public distrust of conventional GMOs might bear for the public acceptance of gene drive technologies.[103] The concern is to ensure the same fate does not befall gene drive technologies, rather than to secure further understandings of the technology or the implications that it might have for affected communities.

Alternatively, the other reports, less instrumental in their consideration of the ethical qualities of gene drive technologies, tend to assume that public participation procedures can overcome any ethical concerns that might exist.[104] This is problematic for a number of reasons. In the first instance, it presupposes that we do in fact know who it is that we ought to be consulting – that we can correctly identify populations of target agents. It is far from clear that our present understandings of gene drive technologies enable us to do any such thing. Secondly, it assumes that the information we are able to provide to those persons is sufficient to enable them to make meaningful decisions. The analysis in the Chapters that follow demonstrates that, due to an almost exclusive focus on technical expertise, our ability to identify target agents or the ways in which they might be affected is vastly inhibited. Thirdly, suggesting that community engagement might resolve any ethical concerns assumes that public participation provides a brake on unethical research practices. History is replete with examples that demonstrate that that is not the case and, as Chapter Seven will demonstrate, exploitation with the consent of the exploitee is still exploitation! As such, current accounts of gene drive technologies eschew substantive ethical enquiry that might condition our understanding of the technologies and its implications for the affected ecosystems and human communities.

[103] The Australian Academy of Sciences (n78) 8.
[104] NASEM (n25) 80-81.

The Chapters that follow focus on how the ways in which we frame technologies impact the way in which we go about regulating them. The basic claim sustained throughout this thesis is that the technical discourses currently privileged in discussions of gene drive technologies (as seen is this Chapter) construct an inadequate understanding of gene drive technologies as a regulatory object – one that fails to properly account for the overflows that the technology might generate and those persons that the regulation should strive to protect. What follows then is an argument for embedding the ethical enquiries currently eschewed into the ways in which we structure our understanding and the frames that we build. In short, I argue that those ethical arguments are vital to developing descriptions of new technologies as regulatory objects.

CHAPTER THREE: THE ROLE OF FRAMING IN DESCRIBING REGULATORY OBJECTS

This thesis focuses on the ways in which legislation frames novel technologies. It considers the ways in which we currently build frames. It thinks about how those frames *ought* to be built. It asks questions about how we might tell good frames and bad frames apart. It describes the hazards of deficient frames and extolls the virtues of frames that fit. However, before such an analysis might be pursued, the relevance of framing must be made out. As such, this chapter provides lawyers with the reasons for which they ought to care about framing.

Before the relevance of framing can be brought out, some explanatory work is required and, to that end, this Chapter introduces the work of a number of scholars working in range of disciplines including Science and Technology Studies (hereafter "STS") and Sociology. The work of STS scholars and sociologists discussed here demonstrates that the way a technology is framed by law has implications for the ways in which these technologies interact with the material world, and the lives that they enable us to lead. This Chapter details the manner in which their work might help to reveal the complexity of gene drive technologies, and the demands that this complexity places on lawyers thinking about regulation.

First, I introduce the work of Sheila Jasanoff and the 'Idiom of Co-Production', arguing for an understanding of science and technology and social orders as mutually constituted.[1] Once the importance of this observation has been made out, we move on to think about the way in which the realities of co-production are significant to thinking about how we conceptualize novel technologies for the purpose of regulation and how co-production conditions our knowledge production practices. As such, Section Two describes the relevance of Michel Callon's work on

[1] Sheila Jasanoff, 'The Idiom of Co-Production' in Shelia Jasanoff (ed) *States of Knowledge: The Co-Production of Science and Social Order* (Routledge 2004) 3; Sheila Jasanoff, 'Constitutions of Modernity: Science, Risk and Governable Subjects' in Maria Weimar and Anniek de Ruijter (eds) *Regulating Risks in the European Union: The Co-Production of Expert and Executive Power* (Hart Publishing 2017).

'hot situations' and 'framing'.[2] In this way, Section Two provides a way into discussions about the sorts of questions that lawyers ought to be asking when developing an understanding of the technologies that they are regulating, as well as a way to put technological complexity 'on screen'.

Building on the analytical framework described in Section Two, Section Three develops an argument for lawyers to legislate with an explicit awareness of the 'framing' process. It is argued that only in engaging in framing can lawyers be said to exercise choice in co-production, thus shaping the way in which science and the social world are mutually constituted. Part of this analysis asks what exercising choice in co-production requires of lawyers, and discusses, albeit briefly, the impact of deficient understandings of public participation within this process.

Section Four demonstrates the ways in which the lawyers engaging in framing might highlight some of the heretofore overlooked complexities of gene drive technologies. In doing so, I highlight the way in which received knowledge practices and their interaction with regulation obscure an important range of concerns and values. Put simply, the claim here is that drafting legislation with an explicit recognition of the importance of framing practices builds frames more appropriate to the technologies that they are trying to represent and manage. In turn, more appropriate frames help us to build safer, fairer worlds.

Section Five goes on to detail the ways in which the process of framing implicates a range of core legal concerns. For instance, I chart the ways in which how we choose to frame a technology has implications for major themes of legal scholarship, including the correct allocation of responsibility. Furthermore, I observe the interaction between the ways in which legal culture informs our framing of technology and the ways in which aspects of technology can effect changes in legal culture.

The final section of this Chapter, Section Six, signposts where the reader might expect the theme of frames and framing to recur and shape the arguments appearing in subsequent chapters.

[2] Michel Callon, 'An Essay on Framing and Overflowing: Economic Externalities Revisited by Sociology' (1998) The Sociological Review 244.

1. The Idiom of Co-Production

In *States of Knowledge*, Sheila Jasanoff introduces us to the idea that "the ways in which we know and represent the world (both nature and society) are inseparable from the ways in which we choose to live in it."[3] This is the idiom of co-production that recognises the mutually constitutive nature of technology and society. The understanding that Jasanoff builds eschews technological determinism's guarantee that it is technology that drives and is responsible for changes and developments in social structures and cultural values. Furthermore, Jasanoff's account of co-production rejects the claim that human knowledge of the natural world and technology is entirely a matter of social construction. Instead, Jasanoff outlines a middle place between technological determinism and social constructivism. Co-production as a middle ground recognises the social aspects of cognitive commitments brought to bear on the production of knowledge of the natural world and material world around us, whilst also embracing the 'epistemic and material correlates of those social formations'.[4] As such, co-production provides a means of accounting for and interpreting the feedback that exists between our knowledge of the world and the ways in which societies (and even individuals) operate.

For example, Charis Thompson describes the way in which the decision to downgrade elephants' conservation status from endangered to manageable resulted from the emergence of a new pan-African identity, capable of facilitating joined-up conservation practices across a range of conservation sites.[5] The decision was not, as a technological determinist might assume, driven purely by a scientific understanding of elephant biology, or population modelling derived from mathematics. Instead, the decision was predicated on an understanding of the natural world, tempered by the realities of local cultural forces and social organisation. In this way the decision

[3] Jasanoff (n1) 3.
[4] Ibid.
[5] Charis Thompson, 'Co-producing CITES and the Elephant' in Sheila Jasanoff (ed) *States of Knowledge: The Co-Production of Science and Social Order* (Routledge 2004) 67.

represents well the feedback and interdependence between scientific understandings of the natural world and the actualities of the social world characteristic of the theory of co-production.

What then, are the upshots of recognising the co-production of science and the social order? In the first instance, a co-productionist account provides a thick description of the phenomena in question, because the descriptions that it renders are imbued with the social, political and cultural contexts within which understandings of technology are developed.[6] Developing thick, and therefore context-informed, descriptions in areas of high technological complexity aids the task of lawyers in building regulatory responses, rather than confining descriptions of technology to technical language and technical understandings. Secondly, a co-productionist account helps 'make sense of emergent phenomena' because it helps to show how certain conceptual and/or cultural frames come to dominate and how they in turn shape the range of relevant concerns. Thirdly, the co-productionist account helps us recognise and make sense of entrenched differences within societies grappling with the same phenomena but to quite different effect. For instance, co-production helps us to understand why, in the face of political challenges, the European Union and Brazil (amongst others) took such divergent approaches to the regulation of genetically modified organisms.[7]

However, alongside the descriptive and explanatory merits of the co-productionist account come significant methodological commitments. When thinking about technologies and what we ought to do with them, a co-productionist account requires us not just to ask questions about the technology in a social cultural vacuum. Instead the co-productionist's methodology requires us to ask questions about human identities, institutions and discourses too, not forgetting the feedback between them and our advancing understanding of the technology. This is a challenge that this

[6] Clifford Geertz, 'Thick Description: Towards an Interpretative Theory of Culture' in *The Interpretation of Cultures* (Basic Books 1973).

[7] To observe the divergence of approach compare: Marine Friant-Perrot, 'The European Union Regulatory Regime for Genetically Modified Organisms and its Integration into Community Food Law and Policy' in Luc Bodiguel and Michael Cardwell (eds) *The Regulation of Genetically Modified Organisms: Comparative Approaches* (Oxford University Press 2010) and Rosaria Silva Gilli, 'Genetically Modified Organisms in MERCOSUR' Luc Bodiguel and Michael Cardwell (eds) *The Regulation of Genetically Modified Organisms: Comparative Approaches* (Oxford University Press 2010).

thesis takes up. When thinking about how we ought to regulate gene drive technologies, this thesis examines the aspects of ourselves, our societies and our legal responses that condition our understanding of both the nature of the problem and the range of available solutions that we conceive of. In no small part, this thesis argues that it is ethics that holds the key to achieving this contextualisation, recognising and formulating the questions that we ought to be asking. This claim is one that I return to in Section Six of this Chapter.

Secondly, and as Jasanoff puts it, '… co-production blurs the very distinction between metaphysics and epistemology, showing how our knowledge of things as they are relates to earlier choices about how we wish to know things in the first place'.[8] As such, we are required to revisit and revise the conceptions we develop as the fulcrum of our enquiry is continually set and reset between metaphysical and epistemological concerns.

In turn, the co-productionist's methodological commitments give rise to a number of ways of making sense of and deploying our newfound understanding of the mutually constitutive nature of technological phenomena and social orders. The first is to say that co-production is just an 'analyst's category'.[9] That is to say, it is merely an analytical approach that, much like technological determinism and social constructionism, sits in the analyst's toolbox to be taken out and used when a theoretical orientation is required. Alternatively, we might argue that co-production provides more than analytical power and instead is capable of providing action-guiding force. In this sense, Jasanoff notes that we might consider co-production a 'strategic instrument in the hands of knowledgeable social actors'.[10]

As such, the co-productionist account provides something more than an account of how scientific understandings and social orders come to be – it offers a chance to reflect on how science and the social order ought to be and how, given the fact of co-production, those 'States of Knowledge' might be realized. Jasanoff offers little with regard to what 'strategic intervention' in

[8] Jasanoff (n1) 274
[9] Jasnoff (n1) 281.
[10] Ibid.

the co-productionist paradigm might look like, although does note that the possibility of such an implication of the co-productionist account merits further attention.[11] Section Three below explores how co-productionist accounts might facilitate strategic intervention in the mutual constitution of science and social orders or, in other words, how we might give meaning to 'choice' in the process of co-production.

Before that can be done however, Michel Callon's description of frames and the framing process must be introduced. Only once the idea of frames and framing have been laid out can we begin to trace the ways in which lawyers, through the regulatory regimes they construct, might be said to be capable of exercising choice in co-production and, therefore, the ways in which science and the social order are mutually constituted.

2. Callon's Understanding of Framing

In his 1998 essay, Michel Callon offers a description of 'framing', which he describes as the process of identifying, measuring and containing 'overflows'.[12] Callon's essay advances a sociologist's response to market economics and, as such, the term 'overflow' shares some similarity with the economist's conception of an 'externality'. In providing an introduction to externalities and overflows for his sociologist colleagues, Callon provides two classic examples. In respect of negative externalities, Callon describes the factory belching waste pollution out into the local countryside at the cost of its inhabitants, who must pay to protect their homes, crops and livestock from the noxious fumes. The factory owners bottom line remains unaffected by their polluting conduct, and so there exists no incentive to remedy the harm to locals who exist quite outside of the economic relationships within which the factory exists. As such the costs generated by the factory remain 'external'.

As Callon goes on to suggest, not all externalities impose economic burdens on external third parties. Instead, externalities or overflows might be positive – providing third parties

[11] Ibid.
[12] Michel Callon, 'An Essay on Framing and Overflowing: Economic Externalities Revisited by Sociology' (1998) The Sociological Review 244.

economic benefits – as is the case in the context of researchers in the pharmaceutical industry gleaning useful information from their competitor's patent applications. Furthermore, our understanding of overflows need not be limited to economic externalities alone. Callon notes that overflows need not be understood exclusively as financial or economic benefits and burdens.[13] Instead, overflows might constitute a setback (or advancement) to an individual's or community's well-being, broadly defined. Callon himself gives examples of non-economic overflows such as a street subjected to high decibel performances of their teenage neighbour's latest musical *idée fixe*.[14] In this way, Callon provides us with the language to describe the effects of gene drive technologies, whether benefit or burden. As such, in what follows throughout this thesis, attention is shifted from identifying 'risks', 'hazards' and 'benefits', to instead identifying 'overflows', thus avoiding the normative connotations that those now specialist and technical terms bring with them.

For Callon, then, the exercise of framing concerns the very process of identifying, measuring and preventing the overflows that would otherwise obtain. Thus, in order to draw up a frame for any given phenomena, we must be able to do three things. Firstly, we ought to be capable of identifying what Callon calls the 'source agents'. Referring back to the factory example, the source agents would be the factory owners and those with whom the factory owners interact in the advancement of their manufacturing operation. Next, we ought to be capable of identifying the 'target agents' – again, referring back to the factory example, the target agents are the affected inhabitants of the local countryside. Finally, we ought to be able to identify and measure the range of potential overflows. In some situations, or scenarios, these three pre-conditions of the framing process are easily fulfilled. These situations are described by Callon as follows:

> In 'cold' situations, on the other hand, agreement regarding ongoing overflows is swiftly achieved. Actors are identified, interests are stabilized, preferences can be expressed, responsibilities are acknowledged and accepted. The possible world states are already known or easy to identify: calculated decisions can be taken.[15]

[13] Ibid 246.
[14] Ibid.
[15] Ibid 261.

A paradigmatic example of a cold situation is an agreement governed by a contract. As Callon notes, in the context of a contract, all of the actors are identified, their interests have been negotiated and stabilized, the preferences of the actors have been put on the table and the responsibilities of the actors have been acknowledged and agreed upon. In contrast, we also face 'hot situations':

> In 'hot' situations, everything becomes controversial: the identification of intermediaries and overflows, the distribution of source and target agents, the way effects are measured. These controversies, which indicate the absence of a stabilized knowledge base, usually involve a wide variety of actors. The actual list of actors, as well as their identities, will fluctuate in the course of the controversy itself and they will put forward mutually incompatible descriptions of future world states. [16]

As an example of a hot situation, Callon refers to the 'Mad Cow Disease' crisis in 1990's Britain.[17] The range of actors party to that particular crisis fluctuated from one day to the next. Some weeks it was the concerns of vets, farmers and feed manufacturers that carried the day. In others it was the concerns of politicians, outraged publics and the media which dictated the direction of discourse on the issue. At the same time, no stabilized knowledge base regarding prion disease and its transmission existed and those party to the debate could not agree on either the facts, or the decisions that ought to be taken. However, much of the discussion below describes the emergence of gene drive technologies and debates surrounding their proper regulation as characteristic of 'hot situations' and Section Four develops this analysis further. For now, it serves to recognise that 'hot situations' can, by certain means, be cooled down and thus framed. The process of cooling down and, thus, rendering the relevant technological phenomena amenable to framing, oftentimes requires two things: that scientists spend a significant amount of time working with non-specialists and significant investment in knowledge gathering.[18] We return to these themes repeatedly throughout this thesis.

Framing, then, requires sifting through an oftentimes vast range of knowledge claims, many of which will be contradictory or competing, in order to determine which knowledge claims ought

[16] Ibid.
[17] Ibid.
[18] Ibid 262.

to condition our conception of the phenomena in question (in our case, gene drive technologies) and the range of legitimate responses to them. In this way, then, we can recognise the relationship between co-production and framing, with the framing process playing a crucial role in determining the end result of the mutual constitution of technology and the social world.

The frame that we choose in order to understand gene drive technologies conditions the adverse effects or overflows that we consider relevant, and therefore seek to manage, control or avoid through regulation. Chapter Four argues that the current scheme of regulation proposed for gene drive technologies fails to identify a broad range of relevant overflows and, thus, the way that it frames the technology is too narrow. Furthermore, the frame that we choose plays a role in identifying whose interests it is we think matter when it comes to developing and controlling the technology and its overflows. Interestingly, the current scheme of regulation takes almost no position on this issue at all. Finally, the frame that we choose stipulates those agents or organisations we consider responsible for avoiding or preventing the overflows that we consider relevant.

3. Framing: Giving Meaning to Choice in Co-Production

Section One of this Chapter provided a description of the idiom of co-production. Section Two provided a description of Michel Callon's account of the process of 'framing'. Whilst Callon's particular interest was the process of framing and, indeed, reframing in the market context, his lessons bear a more general applicability. This section argues that in thinking closely about how we as lawyers frame technologies (in the way that we identify the relevant source agents, target agents and overflows) there lies a powerful means of choice, or strategic intervention, in the process of co-production. In other words, thinking carefully about the frames that we adopt gives directionality to co-production, shaping the forms and nature of the technology and the society as they are mutually constituted. The ways in which we gather, structure and understand knowledge bear implications for our understandings of the material world and social orders, which in turn shapes our conception of right action in response to the technological and social challenges we

face. The frames that we adopt shape our individual, institutional and infrastructural responses to the problems we are attempting to tackle. As such, developing robust frames can be one of the most important things that we as lawyers do in ordering the world around us. In the context of gene drive technologies, the understandings we arrive at will inform the regulatory decisions we make with regards to the types of gene drive we permit and the conditions we place on their development and use.

A number of scholars, particularly those working in environmental law, have highlighted the relationship between lawyers' understandings of technology, legal frames and the articulation and attainment of policy objectives. For instance, in his article on fracking, Christopher Hilson develops an analysis of the frames adopted by social movements, governments and lawyers and the ways in which those frames are accommodated or excluded by the relevant planning regimes.[19] In this way, Hilson develops an approximation of the distance between frames constructed by lawyers and the frames constructed by non-legal actors, noting the ways in which the legal and regulatory frames place many community constructed frames beyond administrable processes.[20]

Furthermore, and again in the context of environmental law, and fracking in particular, Elen Stokes notes the practical implications of lawyers' understandings of their own frames.[21] For instance, where a process is understood to be analogous to existing and adequately regulated techniques, a frame of regulatory sufficiency (or, in Stokes' language, 'regulatory domain') prevails. In these situations, non-intervention and maintenance of the regulatory *status quo* are preferred by lawyers and policy maker alike. However, in the fracking context, Stokes notes the co-existence of a second contradictory frame – one that describes the products of fracking as something apart from existing fuels, and therefore requiring regulatory reform. Stokes goes on to demonstrate how

[19] Chris Hilson, 'Framing Fracking: Which Frames Are Heard in English Planning and Environmental Policy and Practice?' (2015) Journal of Environmental Law 177.
[20] Ibid 201-202.
[21] Elen Stokes, 'Regulatory Domain and Regulatory Dexterity: Critiquing the UK Governance of 'Fracking' (2016) The Modern Law Review 961

these competing conceptions of the technology as framed by lawyers and regulators work together to accomplish governmental policy objectives.

Beyond fracking, we observe the connection between lawyerly frames and co-production in the chemicals context. In Fisher's work we can see the simultaneous overcomplication and oversimplification of understandings of technology that comes with the adoption of multiple frames in respect of the same technological phenomena.[22] Fisher's article demonstrates that in the regulation of chemicals, chemicals themselves have been constructed as divergent regulatory objects – as risky objects under the US Toxic Substances Control Act, as market objects under EU REACH regulations and as scientific objects under various Green Chemistry initiatives.[23] Fisher's analysis demonstrates explicitly the role of framing in the co-production of science and the social order and, importantly, the significance of the legal and regulatory framing of the technology in this process in particular. Put simply, in the context of chemicals regulation, it is the legal and regulatory construction of the phenomena in question that dictates the appropriate regulatory response. In this way then, we can straightforwardly observe how lawyerly framing of technologies affects the place that the technology has in the world. The frames that lawyers construct can provide conclusive answers to whether certain technologies ought to be used and, if so, how they ought to be regulated.

As with all things, there are good frames, less good frames and downright bad frames. Roger Brownsword's taxonomy of 'Regulatory Connection', further expanded on in Chapter Four, provides one means of assessing the precision and fidelity of the legal and regulatory frames that we build.[24] Adopting Brownsword's model, Chapter Four develops an argument for conceiving of GMO Regulation as a downright bad frame from which to start our enquiry into the proper regulation of gene drive technologies. Chapter Five argues that public health law provides a less

[22] Elizabeth Fisher, 'Chemicals As Regulatory Objects' (2014) Review of European Community and International Environmental Law 163.
[23] Ibid 166-170.
[24] Roger Brownsword, *Rights, Regulation and the Technological Revolution* (Oxford University Press, 2008) 160-184.

problematic, yet still non-ideal, frame from which to develop the regulation of gene drive technologies. However, beyond discrete Chapter boundaries, a strand of argument running throughout this thesis asks lawyers to conceive of themselves as crucial to the development of these frames – crucial to sifting through our current understandings of the technology for those features that are relevant or significant and to identify what we need to understand better.

Recalling Stokes, this process takes many forms but oftentimes proceeds from an assessment of whether the technology in question is analogous to a pre-existing phenomenon that we consider ourselves to have a sufficient understanding of. However, such a starting point requires a well-developed and technically competent understanding of the technology before, as a matter of framing, we can say whether or not they are like pre-existing techniques and if not, why not. Furthermore, we ought to note that 'technical' similarities need not reflect similarities of legal or regulatory significance – borrowing here from Theodore Porter's conception of the 'technical' as those things inaccessible to public reason.[25] For example, early iterations of gene drive technologies were developed using the 'zinc-fingers' technique germane to all techniques of genetic modification.[26] As a matter of process, the creation of these gene drive constructs was 'technically' identical to non-gene-drive GMOs, but the technical similarity was not indicative of the need to regulate them quite differently. In the same vein, technical differences do not always warrant divergent legal or regulatory responses.[27]

In many ways, such a plea bears no great novelty. At its simplest, it is a plea for lawyers to adopt more holistic and broader frames, developed through robust engagement with the actualities of the technology they are trying to regulate and the science behind it. Fisher's calls for 'collective epistemic responsibility' reflect the same impulse, recognising that 'scientific uncertainty is not just

[25] Theodore M Porter, 'How Science became Technical' (2009) Isis 292, 293.
[26] Vanessa M Macias, Joanna R Ohm and Jason L Ragson, 'Gene Drive for Mosquito Control: Where Did It Come from and Where Are We Headed?' (2017) International Journal of Environmental Research and Public Health 1006.
[27] L Bennett Moses, 'Sui Generis Rules' in GE Marchant, BR Allenby and JR Heckert (eds), *The Growing Gap Between Emerging Technologies and Legal-Ethical Oversight: The Pacing Problem,* vol 7, International Library of Ethics, Law and Technology (New York, Springer, 2011) 77.

a data gap, but refers to a range of different technical, methodological, epistemological, and ontological uncertainties in the practice of science.'[28] Thus, Fisher calls for political communities to recognise their duty to determine the conditions under which knowledge is produced, the way in which it is used and how we understand it to be reliable and accountable. Furthermore, Brian Wynne raises similar concerns when he notes that:

> We have learnt from the detailed analysis of the creation of scientific knowledge over the past twenty years or so, that many of the intellectual commitments which constitute that knowledge are not completely validated, not fully determined by empirical nature. Always central to the process are not just uncertainties in the form of imprecision (which, it is assumed, will be narrowed down by more research), but indeterminacies, for example, as to whether things are classified as the same or different, and on what specific properties or criteria. The purely technical aspects of such intellectual commitment merge with epistemic questions as to why we are constructing such knowledge anyway.[29]

As such, if lawyers are to engage with the framing of the technologies they are charged with regulating, attention must be paid to the contemporary and entrenched knowledge practices. The knowledge claims lawyers are presented with by the scientific community play a large role in constructing the frames we use to understand emerging technologies. However, lawyers must pay attention to the provenance of those claims, as well as from where else knowledge claims capable of informing the regulatory frame might be derived.

Asking lawyers to exercise choice in co-production through framing, or, somewhat more appealingly, asking them to take collective epistemic responsibility is one thing, but prescribing how one might go about it is quite another. One response is to demand a high level of scientific expertise of decision makers.[30] However, as Fisher suggests, not only is this not what is required but it may in fact serve to exacerbate the dominance of overly narrow and technical frames in regulatory decision making as it serves to obscure the reality of co-production.

Another response to demands for lawyers to take an active role in the framing of technologies is to recommend engagement with relevant publics. If calls for collective epistemic

[28] Elizabeth Fisher, 'Sciences, Environmental Law, and Legal Cultures: Fostering Collective Epistemic Responsibility' in Emma Lees and Jorge E Vinuales (eds) *The Oxford Handbook of Comparative Environmental Law* (Oxford University Press 2019) 749, 753-754.
[29] Brian Wynne, 'Uncertainty and Environmental Law' (1992) 2 Global Environmental Change 111, 126.
[30] Fisher (n28) 755.

responsibility are motivated by a desire for lawyers to avoid overreliance on narrow technical frames when making decisions about how best to regulate a technology, then perhaps public participation can play a role in broadening those frames by bringing a range of otherwise overlooked knowledge claims to the table? If, as suggested above, framing requires lawyers to sift through a range of knowledge claims and decide which of them are relevant to understanding the salient features of the technology that they are trying to regulate, then public participation provides a means of gathering a broad range of knowledge claims through which to sift.

Indeed, scholars have nodded toward public participation as the weapon of choice in the fight against scientific uncertainties that manifest as deficits of reason within the arena of political decision-making and public reason.[31] Thus, in some of the literature, we see suggestions that engaging publics might constitute an adequate means of taking epistemic responsibility in regulatory decision making. For instance, Jenny Steele notes the role of public participation as an aid to problem solving in key areas of scientific uncertainty.[32] In Steele's view, the increased calls for participatory processes in European Union Environmental Law, as evidenced by instruments such as the Aarhus Convention, reflect more than a concern for democratic decision making. Instead, for Steele, participatory processes recognise publics as a source of values, knowledge and solutions capable of enhancing the quality of regulatory decision making.[33] Steele notes the GMO context in particular as a crucible within which the utility of public participation as a response to scientific uncertainty was tested and borne out.[34] Whilst emphasizing the role of public participation in reversing the European Union's perceived democratic deficit, Maria Lee also argues for the richer perspectives that public participation provides in improving decision making processes.[35]

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[31] Ibid.
[32] Jenny Steele, 'Participation and Deliberation in Environmental Law: Exploring a Problem Solving Approach' (2001) Oxford Journal of Legal Studies 415, 416.
[33] Ibid 441.
[34] Ibid 422.
[35] Maria Lee, *EU Environmental Law, Governance and Decision-Making* (Hart 2005) 202.

However, I caution against equating the development of public participation processes with the practice of taking epistemic responsibility. Whilst public participation in policymaking is important, and no doubt crucial in the context of safe and fair use of gene drive technologies, claims for public participation are no less problematic than bare calls for lawyers to engage in framing. Unspecified calls for public participation demand lawyers listen to the widest range of possible voices, without providing any conception of what it is that they are listening for. Whilst Lee might ground the utility of public participation in its ability to bring a range of otherwise overlooked values to the table, little guidance is offered with regard to how this wider range of values ought to be organised, prioritized or implemented in the context of regulatory decision making.[36]

To be sure, collective epistemic responsibility cannot be achieved by weighing all knowledge claims and according them equal weight and importance. Rather, that would be an exercise of collective epistemic collation or, if using language of framing, a matter of gathering together all possible frames, heaping one on top of the other, instead of building the most robust one. Recalling Hilson, it is not hard to see the difficulties associated with attempts to record and accommodate all of the various frames rendered by social movements, government policy makers, lawyers and lobbyists concerned by fracking. Thus, whilst public participation is a necessary antecedent to the building of robust regulatory frames, public participation itself is not a silver bullet that when ticked off the checklist ensures that the resulting frame is sufficiently broad.

Recognising this problem, Chapters Six and Seven develop an argument for ethics as central to both framing and public participation. The aim of these chapters is to demonstrate that ethics can provide a starting point for drawing out the salient features of the technology that ought to inform legal and regulatory framing. Understanding the ethical qualities of the technologies that we study illuminates their place in and effect on the material world – identifying overflows and

[36] Ibid.

target agents that might otherwise be overlooked. In many ways ethics helps to feed the legal imagination that lawyers require for the development of robust frames. Similarly, I contend that attention to ethical concerns hone the lawyer's ear to the claims that they ought to listen out for in participatory processes. Concerns for environmental ethics and exploitation play a role in identifying the relevant target agents, source agents and unanticipated overflows as well as providing substantive constraints on participatory processes. As such, ethics plays a vital role in illuminating *and* constraining the framing process. Ethical enquiry aids lawyers in framing by providing a conception of what it is that we are looking for when sifting through the knowledge claims adduced by various different parties. That is, substantive ethical enquiry gives us some sense of which overflows, target agents and source agents ought to be ruled in and ruled out when it comes to building the frame.

4. Gene Drive Overflows

As noted in Section Three above, Callon argues that hot situations are characterised by controversies in (a) the identification of intermediaries and overflows; (b) the distribution of source and target agents; and (c) the way the effects are measured. This section seeks to identify the range of overflows, target agents and source agents implicated by gene drive technologies, many of which go overlooked by the current scheme of regulation. Furthermore, I chart the challenges that we are confronted with when trying to identify any of the features Callon calls for. As such, this section describes the controversies that arise in the context of gene drive technologies and, in doing so, attempts to render a description of the technology amenable to legal thinking.

4.1 Controversies in Identifying Intermediaries and Overflows

4.1.1 Challenges in Gathering Necessary Data

One of the greatest challenges facing the framing of gene drive technologies is the lack of a sufficient and stabilized knowledge base. In relative terms, gene drive technologies are still in their infancy and our understandings of them shallow. This is perhaps best demonstrated by the fact that up until recently understanding of gene drive technologies was so limited that on a number

of occasions scientists accidently, or inadvertently, created gene drives whilst working on different projects.[37] Relatively little is understood about the ecological effects that the release of gene drive technologies might have and even less is understood about their potential effects on human communities. This lack of a sufficient and stable knowledge base is attributable to a number of causes. In the first instance, relatively few researchers are engaged in developing our understandings of gene drive technologies. Secondly, the nature of the technology itself bears challenges for the safe and effective gathering of reliable and useful information. These two concerns will be addressed below in turn.

At the time of writing five teams of research scientists are working on the development of gene drive technologies for the control of vector borne disease.[38] This bears two implications – the first relates to the *type* of knowledge we have at our disposal (all of our knowledge is technical) when thinking about framing and the second relates to the *breadth* of knowledge.

Due to the present lack of a specialised regulatory framework for the governance of gene drive technologies all of the information and knowledge that we currently possess has been generated by research scientists alone. As Sheila Jasanoff points out, the knowledge produced by research scientists (as opposed to regulatory scientists) varies in its usefulness when we are required to deploy it in the context of regulatory decision making for new technologies.[39] Whilst regulatory science is concerned with uncovering 'truths' relevant to policy and decision-making, research science or 'basic' science is more concerned with 'truths' of originality and significance.

Although these truths of originality and significance power our technological leaps, few are amenable to utilization in the context of regulatory decision making.[40] Knowing that the genotype coding for male sex might be driven through a mosquito population in X generations is one thing,

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[37] Esvelt K, 'Gene Editing Can Drive Science to Openness' (*Nature World View*, 9 June 2016) https://www.nature.com/news/polopoly_fs/1.20043!/menu/main/topColumns/topLeftColumn/pdf/534153a.pdf Last accessed 5th September 2019

[38] A relatively up to date list of some of the key players in gene drive research is maintained by the Outreach Network for Gene Drive Research and is available at: https://genedrivenetwork.org/#about Last accessed Monday 19th August 2019.

[39] Sheila Jasanoff, The Fifth Branch: Science Advisers as Policy Makers (Harvard University Press 1998) 75.

[40] Ibid.

knowing what implications that bears for the surrounding humans and ecology is quite another. As such, of the knowledge that we do currently possess, relatively little of it is sensitive to the language and concerns of policy makers and lawyers. This is not, however, a mere failure of translation or transposition and it would be wrong to think that we might overcome this disconnect by introducing an intermediary capable of describing the results of basic research in a manner useful to the regulatory sphere. Rather, there exists a pressing need to pursue research and develop knowledge relevant to framing, and thus regulatory decisions.

Secondly, the nature of the technology itself presents challenges to the very process of gathering the information required. Whilst there exist established and excepted modes of research design and method in the context of agricultural biotechnologies, the self-proliferating nature of gene drive technologies challenges existing assumptions around what is required to produce reliable data.

We return to discuss this problem again in Chapter Four in the discussion surrounding the inadequacies of the current regulatory framework for gene drive technologies, but it deserves some discussion here too. Due to the fact that gene drive technologies have the potential to spread throughout all endemic regions without, at present, a means of recalling or stopping them if and when harm arises, there exists a tension between designing safe, well contained trials on the one hand, and gathering reliable data on the other. A number of options have been tabled by actors within the scientific community, ranging from trial releases on uninhabited islands,[41] collecting data from releases into well-guarded hangars, and mocking up entire villages within secure, enclosed and guarded spaces. The more secure we are able to make a trial release by creating safe and secure enclosures, the less reliable the data becomes for want of fidelity to real world conditions. Sterile, secure and well-controlled environments do not reflect the reality of complex and innumerable interactions gene drive organisms will play a part in, in the world at large.

[41] T Harvey-Samuel, K J Campbell, M Edington and L Alphey, 'Trialling Gene Drives to Control Invasive Species: What, Where and How?' in C R Veitch, M N Clout, A R Martin, J C Russell and C J West (eds) *Island Invasives: Scaling Up To Meet the Challenge* (IUCN 2019).

To be clear, whilst certain features of gene drive technologies present problems of Wynnian 'ignorance' or Rumsfeldian 'unknown unknowns', that is not necessarily the issue faced here.[42] Instead, we are dealing in uncertainty - a range of known unknowns which, in making themselves known, might reveal significant and potentially irreversible harms. In short, our ability to identify and measure the overflows that this technology creates, whether in respect of human health, the environment, ecology or the economy is curtailed by the very nature of the technology. This aspect of gene drive technologies presents a sense in which we cannot know what overflows might exist in order to inform our choice of frame and, yet,, acknowledging this reality itself informs the nature of the frame that we as lawyers choose to build.

4.1.2 Overflows Overlooked

Above, we scoped the difficulties associated with identifying some of the more obvious but unrevealed overflows generated by the use of gene drive technologies. The concerns charted above are ones that take a ready place in discourses surrounding the regulation and deployment of gene drive technologies. The overflows described here are somewhat different – they do not form part of the conversation about the 'risks' of gene drive technologies such as those put forward by scientists and discussed in Chapter Two. Instead, these are the overflows that demand the exercise of imagination in order to be brought within the legal frame.

Inquiries into the possibility of harm to either human health or the environment can, at times, be rather narrow inquiries, with this narrowness at least in part dictated by the realities of the scientific method. Thus, when we ask whether gene drive organisms present a threat to human health, we tend to ask questions along the lines of, 'Are the effects of a bite from a gene drive mosquito more harmful than that of a wild-type mosquito?'. Instead, and more importantly, we ought to be asking more difficult questions about the effects of a multiplicity of interactions as

[42] Brian Wynne, Uncertainty and Environmental Learning' (1992) 2 Global Environment Change 111; Donald Rumsfeld, Department of Defence News Briefing – Secretary Rumsfeld and Gen. Meyers, United States Department of Defencehttps://archive.defense.gov/Transcripts/Transcript.aspx?TranscriptID=2636 Last accessed Monday 19th August 2019.

they occur within complex, open systems. We should ask whether reducing the population of anopheles vectors might cause a boom in the population of another disease-carrying species and therefore, whilst reducing the burden of malaria, increase the burden of any of a range of other tropical diseases. Similarly, with respect to environmental or ecological damage, research is focusing on the role of the target organism within food webs and their ecological niche. These are the overflows that we pay attention to when we frame concerns about gene drive technologies as concerns for human health and the environment.

However, whilst such a focus is indeed important it obscures our view of other important and, perhaps in some cases, equally impactful overflows. When we ask about how gene drive technologies might affect health and/or the environment, we often fail to take notice of the cumulative, aggregate or long-term effects the technology might have. Marie Lee makes a similar suggestion in respect of the regulation and framing of the harms caused by GMOs.[43] To be sure, history is littered with monuments to our folly and our failures to anticipate overflows. Whether the invasion of cane toads in Australia,[44] the legacy of the pervasive use of asbestos[45] or the ozone popping effects of chloro-fluoro-carbons,[46] we need not look too far to recognise the harms that follow the adoption of overly narrow frames. Oftentimes, these failures of framing result from failure to acknowledge the interactions between technology, material worlds and cultures within which they are deployed. Other times, these failures are the result of a frame taking only a short-term view. This section seeks to describe some of the overflows more overlooked, yet essential for developing a robust and well-constructed frame within which lawyers might understand and respond to gene drive technologies.

[43] Maria Lee, 'Beyond Safety? The Broadening Scope of Risk Regulation' (2009) Current Legal Problems 242.
[44] Christopher Jolly, Richard Shine and Mathew J Greenlees, 'The Impact of Invasive Cane Toads on Native Wildlife in Southern Australia' (2015) Ecology and Evolution 3879.
[45] Jock McCulloch and Geoffrey Tweedale, *Defending the Indefensible: The Global Asbestos Industry and Its Fight for Survival* (Oxford: Oxford University Press 2008).
[46] Sharon L Roan, *Ozone Crisis: The 15 Year Evolution of a Sudden Global Emergency* (John Wiley & Sons 1990).

4.1.2.1 Loss of Acquired Immunity

The first overflow noted here responds precisely to concerns regarding frames with short term views. If gene drive technologies are to be rolled out successfully in the battle against vector-borne diseases, then they must be both effective and available in the long term. In the case of malarial disease, this concern is particularly acute. Individuals residing within endemic regions do, over time, build up immunity to the malaria-causing plasmodium parasite. This is why the high-risk groups for serious and fatal malaria are the under-fives and migrant populations – in other words, those who have not acquired immunity to the disease.[47] As such, if gene drive technologies were to be successfully and effectively deployed and then, through either technological or infrastructure failure become unavailable, large populations of disease naïve individuals – those without acquired immunity – would be vulnerable to acute and fatal presentations of the disease.[48]

4.1.2.2 Human Behaviour

Overflows are often overlooked when we fail to consider the apparent and varying needs and interests of the communities within which an intervention is introduced. *Ex ante* inquiries into the overflows that we might anticipate often neglect to consider the effects of self-interested behaviour on the part of agents affected by the intervention in question. In many ways, overflows motivated by self-interest represent the paradigmatic externalities discussed by Callon in his essay and economists more generally in the wider literature.[49]

In other words, we fail to consider the seemingly unpredictable, yet rationally explicable behaviour of human beings interacting with and responding to the intervention implemented. The behaviour of human actors within the system can, and does, have real consequences for the success or failure of whatever intervention it is that we have in mind. Further, there are examples of the

[47] See: World Health Organisation, 'Malaria: High Risk Groups' https://www.who.int/malaria/areas/high_risk_groups/en/ Last accessed 26th June 2019. Note: Infants under 3 months of age benefit from acquired immunity conferred by their mothers.
[48] H Reyburn, C Drakeley, 'The Epidemiological Consequences of Reducing the Transmission Intensity of *P. falciparum*' in C Boëte (ed) *Genetically Modified Mosquitoes for Malaria Control* (Eurekah/Landes Bioscience 2006) 89–102.
[49] Callon (n2); See also: Garret Hardin, 'The Tragedy of the Commons' (1968) Science 1243.

effects of human behaviour from two contexts close in kind to that examined here: public health interventions for malaria and species control interventions.

Bed net distribution programmes have formed a large part of the public health response to malaria, however there is mounting evidence that suggests the misuse of insecticide impregnated bed nets has implications for both human health and the environment. Various studies have addressed the effects of bed nets used for fishing rather than for protection from mosquitos, noting adverse consequences for both disease burden with the human population as well as negative implications for fish stocks.[50] Using bed nets as fishing nets reduces control of vector populations in the fight against malaria whilst at the same time depleting fish populations due to either the fine mesh of the nets removing smaller, juvenile fish from the population, or the insecticide covering the nets proving toxic to the fish.[51] Whilst much of the literature on this issue describes this phenomena as 'unintended', we might instead recognise it as a failure of framing. Whilst such an end point was not intended, that it might have come about would have been knowable had the conception of relevant knowledge been different. Put simply, the framing of bed net use was overly narrow, failing to take into account the needs and interests of the target communities beyond those associated with the burden of malarial disease. Conceiving of bed net users as little more than potential malaria sufferers narrowed the range of knowledge gathered. Such effects might have been prevented altogether had the day-to-day needs and interests of the human communities they affected been considered. Furthermore, adequate community participation would reveal food security to be a greater and more pressing concern than the avoidance of malaria. Had such a hierarchy of interests been taken account of, the misuse of bed nets might well have been anticipated.

[50] Noboru Minekawa, Gabriel O Dida, Gorge O Sonye, Kyoko Futami, and Satoshi Kaneko, 'Unforeseen Misuses of Bed Nets in Fishing Villages Along Lake Victoria' (2008) Malaria Journal 165.
[51] Rebecca Short, Rajina Gurung and E J Milner, 'The Use of Mosquito Nets in Fisheries: A Global Perspective' (2018) PLoS One e0191519.

The use of bed nets for fishing presents an example of a situation in which, due to other outcompeting interests held by those individuals that the intervention targets, the aims of the intervention are at least partially thwarted. Human interactions with measures designed for the control of invasive species present another example of the self-interests of rational actors affecting the efficacy of the intervention in question. Hailed as the first successful mammalian pest biological control program, the Commonwealth Scientific and Industrial Research Organisation released the myxoma virus into the rabbit population in an attempt to curb its vast numbers.[52] As a result, farmers in 1950's Australia travelled from all States in order to collect infected rabbits to release on their own farms in attempt to reduce the abundance of the pest on their land.[53] Similarly, the myxoma virus found its way from England to Ireland by way of intervention from the general public – notably, by posting infected rabbit skins to Irish farmers for them to be rubbed over healthy animals.[54] The literature documenting the spread of myxomatosis describes the human-aided spread of the disease across national boundaries as unintended, unanticipated and accidental.[55] However, this narrative ought to be challenged. Had the interests of farmers been taken account of, this sort of behaviour and its consequences would be straightforwardly predicted. As a farmer with a pest problem in the form of an overabundance of rabbits, it is quite rational to try and get your hands on *the* most effective pest control solution. In that way we can conceive of these overflows not as unanticipated but rather as the predictable by-products of rational self-interest. One need not reflect too long on how such behaviours might complicate the safe and contained release of gene drive technologies. As such, questions of surrounding human interactions with planned manipulations of the material world ought to be questions that reside within a robust, well-constructed frame for the technology.

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[52] Commonwealth Science and Industrial Research Organisation, 'Controlling Those Pesky Rabbits' https://www.csiro.au/en/Research/BF/Areas/Invasive-species-and-diseases/Biological-control/Controlling-those-pesky-rabbits Last accessed 27th June 2019.

[53] -- 'Farmers In Scramble to Beg, Borrow or Steal A Rabbit' The Dubbo Liberal and Macquarie Advocate Friday 16th February 1951, 1. Available at https://trove.nla.gov.au/newspaper/article/131335446/14990216 Last accessed 27th June 2019.

[54] Michael J Conry, The Rabbit Industry in Ireland: 20th Century Snapshots (Michael Conry Books 2016).

[55] Peter Kerr et al, 'Myoma Virus and Leporipoxviruses: An Evolutionary Paradigm' (2015) Viruses 1020.

4.2 Controversies in Identifying the Source and Target Agents

4.2.1 Identifying 'Target Agents'

Whilst the section above focused on overflows that go overlooked, this section focuses on the difficulties associated with identifying target agents. Callon's 'target agents' are those persons either benefited or burdened by the overflows resulting from the 'source agents' proposed activity. In this case then, some time must be devoted to thinking about how we might identify those persons affected by the overflows. This, of course, presupposes that we can indeed draw up an exhaustive list of the overflows – the likelihood of which has been doubted above. However, we might still usefully ask whose interests ought to be brought within the frame and this section aims to draw out the complexities of what might otherwise appear to be a straightforward task.

We know that gene drive technologies have the potential to spread to all populations of the species that they affect, and so all of those persons sharing their environment with the target species might come to experience both the benefits and the burdens that the technology brings. On this expansive view, given gene drives self-proliferating, geographical and political boundary-disrespecting nature, there is a case for conceiving of the relevant class of target agents as all of those persons residing within endemic regions. For example, if we were to ask who might be the target agents in the context of a gene drive designed to eradicate the mosquito carriers of the *Plasmodium falciparum* malaria parasite, if the expansive view is correct, our class of agents would consist of over 2.37 billion persons, occupying a space of over 29.7 million km^2.[56]

On the expansive view, it is the totality of the world's mosquito population that draws the borders of our frame. Alternatively, we might take a restrictive view and conceive of the relevant class of target agents as only those residing within the locale of the gene drive release site. If the

[56] Beatrice Autrino, Alice Noris, Rosaria Russo and Francesco Castelli, 'Epidemiology of Malaria in Endemic Regions' (2012) Mediterranean Journal of Haematology and Infectious Diseases e2012060. There might even be a case for arguing that this expansive view does not account for all relevant agents, if we take into account the possibility of horizontal gene transfer between mosquito species. If for instance, the genetic apparatus that codes for the gene drive system were to move into Plasmodium vivax vector, then all of those living in endemic P. vivax regions might be said to be relevant target agents too.

gene drive organisms were the *Aedes agypeti* mosquito who travel only a few hundred feet over their life time, this restrictive view might well justify us limiting the class of target agents to the geographical area immediately surrounding the release site which in real terms would be, at most, a few hundred persons. On the restrictive view, the flight behaviours of the target species dictate which humans sit both within and without our frame.

However, between the expansive view and the restrictive view there exist a great many other options for identifying our target agents. For instance, we might maintain that the relevant persons or 'target agents' are those residing within 'host communities' – for instance, the village or town within which the gene drive technologies are released. In this case, we trace the contours of our chosen frame along the political boundaries revealed on the maps of the regions concerned. This frame, however, might be too restrictive still – we know that the gene drive organisms themselves will not respect political boundaries, and we can foresee that the organisms will move into the territory of neighbouring towns and villages, bringing with them both their benefits and burdens. If this is the case, then perhaps host communities and their nearest neighbours ought to be considered the target agents. As such, the frame is predicated on a mixture of real-world political boundaries and artifice that flows from our understanding of the way that gene drive technologies behave. In this way, we can recognise that the bases of the frames might vary from 'technical', 'non-technical' or a hybrid of the two where we understand 'technical' bases as those communicated in concepts and language understood only by specialists and therefore, in Theodore Porter's terms, walled off from public reason, intelligible only to experts belonging to a particular scientific specialism.[57]

All of the possibilities for identifying our target agents have so far only taken into account those persons that might, for one reason or another, come into direct contact with gene drive technologies and their benefits and burdens. What about the governments of the states within

[57] Porter (n25) 294.

which gene drive technologies are released? How are they relevant? On the one hand, if gene drive technologies were successful in their elimination of malaria, governments would reap economic benefits of all kinds, no longer having to devote budget, infrastructure and expertise to the control of malarial disease. On the other hand, should gene drive technologies fail, or generate any of a number of adverse consequences for health, the environment or societal values (such as equality) these governments will be turned to for rescue and remedy. As such, we might make the case for including institutions as well as individuals within the frame. In this sense, a range of our target agents might also share the label of 'source agents'. This further complicates the picture – particularly with respect to questions about who ought to bear responsibility for gene drive failures – but we will return to this question below.

4.2.2 Identifying 'Source Agents'

For Callon, the 'source agents' are those who propose the course of action from which the overflows are derived. For example, in the context of a cold situation such as contract formation, the source agents would be the voluntary parties to the agreement. However, in the context of 'hot' situations, as Callon points out, there exists a state of flux in which source agents might become (or also be) target agents, and then revert once again. As he puts it, 'The actual list of actors, as well as their identities will fluctuate in the course of a controversy itself…'.[58] This state of flux accounts for what some might consider a feat of double counting, insofar as a number of agents present at one time or another as a source agent, a target agent, or both.

Who then, are the individuals or institutions that we might think of as the source agents? Could they be the individual researchers, or the research institutions to whom those researchers belong? Could they be those philanthropic organisations that sponsor and fund the research carried out by the aforementioned researchers? Could they be the individuals that make up the communities who agree to the experimental release of gene drives, or perhaps just the

[58] Callon (n2) 260.

representatives of those communities? How about the Governments within the States where gene drive technologies are released – does their permission (or as is more often the case, failure to provide prohibition) for the release of gene drive technologies qualify them as source agents? What of the institutions regulating gene drive research and deployment, either in the host country, or in those countries within which the basic research is taking place?

5. How Framing Affects Things Lawyers Care About

Section Four asked two questions. Firstly, what 'overflows' are relevant for inclusion within our framing of gene drive technologies? Secondly, whose interests are relevant to the framing of gene drive technologies? Having identified a range of possible answers to both of these questions, this section reflects on why the frame that is ultimately chosen ought to be of such keen interest to lawyers. In short, I suggest that the frame that we choose has implications for the things that lawyers care about and issues germane to their practice. As Liz Fisher puts it, 'law has an important role in reframing our understanding of the world and responsibilities in relation to it.'[59] In the simplest terms, the frame we choose as lawyers determines 1) who owes duties, (2) to whom those duties are owed, and (3) what those duties are owed in respect of. However, co-production does not halt there. The answers lawyers consider for these questions in turn affect the overflows, target agents and source agents that are taken account of by the resulting regulatory framework. Those three questions also have implications for other lawyerly concerns, such as what information ought to be provided, and to whom, who bears responsibility for developing necessary capacity and infrastructure, and who ought to bear responsibility should gene drive technologies cause harm. In this way, the three questions described above play an important role in determining the relevance and import of a range of knowledge claims that a lawyer might be confronted by. Furthermore, these three questions can condition the knowledge practices lawyers demand in

[59] Liz Fisher, 'Imagining Technology and Environmental Law' in Roger Brownsword, Eloise Scotford and Karen Yeung (eds) *The Oxford Handbook of Law, Regulation and Technology* (Oxford University Press, 2017).

deciding how best to regulate. As such, these three questions and their answers shape the full range of appropriate regulatory responses to gene drive technologies.

In describing the relationship between law and framing in this way, one might quite reasonably ask why broad questions of regulation should coalesce around these three rather narrow questions – the concerns of regulation can, and very often do, extend far beyond the questions described above. However, whatever theory of regulation one adopts – whether we understand the emergence of regulation and its key actors and concerns as best accounted for by public interest theories, private interest theories or institutionalist approaches – the role that law plays in regulation remains consistent.[60] As Yeung and Morgan note, the relationship between law and regulation is one of facilitation wherein law facilitates the ends of regulation. In their words, we might consider law the Umpire of the regulation game.[61] If this is the case, we can understand regulation, no matter how broad its concerns might be, as adhering to some of the arch concerns of the Umpire that makes play possible. Beyond the Umpire analogy, Hancher and Moran argue that, 'the character of a legal culture mediates the regulatory process, fixing the scope of regulatory space and influencing who gains entry and on what terms'.[62] In this way then, it is clear that some of the core commitments of legal culture as articulated in the three questions described above play a significant role in shaping the contours of the regulatory process and substance.

5.1 Engaging 'Target Agents'

Once our target agents have been identified and brought into the frame, questions remain regarding what duties they are owed. One facet of this complex question relates to how they ought to be engaged in the decision-making process, both with regard to what information they ought to be provided with, and how their wishes ought to be taken into account. However, their very identification bears implications for the way in which we think they ought to be engaged. For

[60] For a helpful introduction to all three of these three theories of regulation see Chapter Two of Bronwen Morgan and Karen Yeung, *An Introduction to Law and Regulation* (Cambridge University Press, 2007).
[61] Ibid 6.
[62] Leigh Hancher and Michael Moran, 'Organizing Regulatory Space' in Hancher and Moran (eds) *Capitalism, Culture and Regulation* (Oxford: Clarendon Press 1989) 271.

instance, the number of persons within any class of target agent has ramifications for what we might consider constitutes good ethical and legally sufficient engagement with that group. Moreover, if we think that our class of agents consists of all those residing within endemic regions, our engagement and participation requirements will be substantially different to those that would be promulgated if we were to take the restrictive view posited above. Given the sheer number of people residing within endemic regions, a lighter touch approach to engagement might be considered appropriate, not least because of the administrative unworkability of a more thorough approach.

In Chapter Five, we will discuss how the law has responded to similar challenges with respect to the identification of target agents and adequate participatory procedures when we consider legislating for the fluoridation of drinking water. However, even once target agents have been identified, it is not clear that we necessarily ought to engage all of the members of the identified class. For instance, if we were to define the class of target agents as all those living within the political boundaries of the host community, it is not self-evident that all of those individuals ought to play a role in the participation processes. It might be the case that all should be consulted, but it might also be the case that it is more culturally appropriate to engage only community leaders or representatives.[63] In this way we can observe the role that law can take in framing, and re-framing, our understanding of gene drive technologies. We can begin to note the mutually constitutive nature of both law and technology and begin to prise apart the practical and normative implications this mutual constitution bears. In this process we see the way that our developing understanding of the technology cuts across already existing, neat legal frameworks and adds further voice to the chorus calling out of the application of legal imagination.

[63] Lawrence Gostin, 'Ethical Principles for the Conduct of Human Subject Research: Population-Based Research and Ethics' (1991) L Med & Health Care 191.

5.2 Responsibility for Gene Drive Failures

This section takes up one of the core commitments of lawyers – particularly tort lawyers or those who, like myself, hail from a medical law background. However, a major theme and concern of legal scholarship focuses on the proper allocation of responsibility. As Peter Cane notes, 'Like "right", "duty" and "property", "responsibility" is a fundamental legal concept, a basic building block of legal thought and reasoning'.[64] The discussion here explores how the frame that we adopt for understanding the technology that we regulate shapes the lawyer's view of how liability for harm might be imposed, if indeed it can be imposed at all. Furthermore, we then observe the manner in which the chosen mode of liability plays a role in framing or re-framing our understanding the technology and the range of appropriate legal and regulatory responses. Observing co-production in practice reaffirms the lawyer's responsibility to engage in the framing process.

5.2.1 Class of Target Agents & Floodgates Liability

Section Four explored the difficulties attendant in any attempt to define the class of source agents and noted a range of technical and non-technical solutions. Whatever solution we adopt has clear implications for the way we conceive of liability. When we take into account that the different solutions available are predicated on somewhat different bases, we should do well to pause over the implications the choice of frame has for our legal intuitions. 'Technical' frames, for instance, offer both the most restrictive and most expansive class of target agents. Identifying the class of target agents as those residing within a few hundred feet of the gene drive release site (reflecting the lifetime flight path of the gene drive organisms) reveals the most restrictive conception with the fewest target agents. Identifying the class of target agents as all those residing within endemic regions (reflecting our understanding of the technologies ability to travel) reveals the most expansive conception with the greatest number of target agents. Non-technical solutions, on the

[64] Peter Cane, *Responsibility in Law and Morality* (Hart, 2002) 1.

other hand, provide something of a middle ground in respect of the size of the class of target agents that they prescribe and yet, as we noted above, these varying understandings of what constitutes the class of target agents can be predicated on quite different knowledge claims – technical, non-technical or even a hybrid.

The conception of the class of target agents adopted has implications for our legal intuitions in respect of legal liability for harms brought about by gene drive technologies. Most obviously, the larger the class of target agents, the more problematic the framework for liability becomes as the law has to negotiate increasingly complex policy considerations. Should the class of target agent be too large, the very possibility of compensating all who suffer harm threatens to stifle the development of the technology altogether. In understanding whether assistance in the form of compensation can, or should, be provided to those who suffer harm, lawyers are invited to make unenviable health-health trade-offs in determining what might be considered 'fair, just and reasonable'.[65]

On the one hand, gene drive technologies promise to save millions of lives but, on the other, they threaten uncertain and potentially unknowable harms. A framework of liability might play a significant role in quelling concerns regarding the possibility of such harms as it brings with it an understanding that where such harms are incurred, the law will seek to place affected individuals in the position that they had been in, prior to the harm. However, imposing liability (if indeed, a source agent or tort duty-holder can be reliably identified) has the potential to halt the development of gene drives altogether, if the costs of liability outstrips the financial viability of research and development. As such, articulating a framework of liability prior to the use of gene drive technologies has the potential to halt their development with the effect of squandering heretofore unprecedented opportunities to conserve life. Here, we observe the reality of co-production as conceptions of the technology and the laws responses are mutually constituted. We recognise the

[65] Caparo Industries PLC v Dickman [1990] UKHL 2.

class of target agents based on a technical understanding of the technology's implications (i.e. how far the technology might spread) and re-scale the contours of that class in light of the realities of legal culture. In practice, for instance, such a working through of the problem might result in the conclusion that the class of target agents consists of those within a certain locality, where the locality has been arrived at on the basis of technical knowledge, overlaid with legal understanding. The category of target agents in this case might well be one not revealed by technical knowledge, non-technical knowledge or legal understanding alone, but is instead constituted by reconciling understandings of all three.

5.2.2 Feedback between frameworks of legal liability and the *ex-ante* management and prevention of overflows

What went above describes a form of co-production in one aspect of legal inquiry – who (if anyone) ought to be compensated if gene drive technologies cause harm. We pause, if only briefly, to note how different aspects of the same legal inquiry inform our overall picture of the phenomena that we face. Put simply, we note how answers to questions such as "who ought to be compensated?", inform our deliberations on broader questions such as "how should this technology be regulated?". For instance, where compensation is able to provide much needed financial assistance to those harmed by a technology (therefore moving injured parties somewhat nearer to the position that they had been in prior to the harm), the risks and hazards we consider it appropriate to tolerate might be somewhat different to those that would be tolerated if no such assistance was available.

6. Narratives of Framing within the Thesis

In this Chapter, I have attempted to introduce one of the core aspirations of this thesis – the provision of a well-grounded argument for lawyers to engage actively in the framing of new technologies when describing them as regulatory objects and drafting legislation for their regulation. Whilst I do not pretend to offer a clear roadmap for the regulation of gene drive technologies in the Chapters that follow, I do offer an orientation for the opening up of those

debates. One of the key contributions this thesis makes is to emphasize the importance of lawyers getting their hands dirty in getting to grips with the technology in question in order to develop robust frames. Lawyers ought to engage in identifying all of the target agents, source agents and overflows that the technology produces instead of relying solely on knowledge claims adduced by technical expertise. This claim is not intended to add to the contemporary clamour denouncing the role of expertise in decision making, it is more to say that there is other expertise that goes overlooked when technical expertise dominates the foreground of regulatory decision making. In that way, and recalling some of the argument made in Chapter One, my claim here mirrors claims made by Theodore Porter, who makes a compelling argument for appreciating the limits and usefulness of different varieties of expertise.[66] Porter asks us to think about the sort of advice we might take from a car mechanic. The car mechanic is, after all, the technical expert we would consult should we need assistance in fixing our car. There are, however, questions the answers to which we might not seek from the car mechanic, even where their technical expertise is capable of rendering an answer of sorts.

Drawing on that analysis further, part of the task of the lawyer in developing robust frames for regulation is identifying when technical experts are indeed proffering technical expertise, or when instead they are offering up mere opinion. As such, this thesis prescribes a way of broadening the frames we use in order to understand technologies beyond narrow technical frames. However, this thesis also attempts to offer a method of building broader frames more ambitious than simply requiring public participation in the hope the diligent publics will bring to our attention overflows that we might otherwise overlook. Instead, it offers an approach that broadens the frames we build by reference to substantive values and substantive ethical enquiry.

[66] Porter (n25).

CHAPTER FOUR: GENE DRIVES TECHNOLOGIES AND THE GMO FRAMEWORK

Whilst relatively little has been written about the regulation of gene drive technologies, a common trend across the literature has been the assumption that, given the lack of other obviously applicable legislation, gene drive technologies ought to be regulated like conventional GMOs.

This chapter takes up the analysis of framing discussed in the last chapter in order to demonstrate that the presumption that gene drive technologies can be regulated by existing regulation covering GMOs is incorrect. Considering gene drive technologies as sufficiently similar to conventional GMOs and regulating them as such is, in itself, an act of framing. However, the frame that results is one that bears little fidelity to gene drive as a technology or the problems that it presents. In highlighting the ways in which the GMO frame fails to fit the contours of gene drive technologies, I discuss how the frame constructed in order to understand GMOs and their regulation came to be constructed. Further, I discuss those features or characteristics of GM technologies that were considered relevant for the purposes of regulation and how their importance came to be constructed. However, an important part of this analysis also considers those aspects of gene drive technologies not accommodated by the frame constructed around GMOs. This analysis takes several steps but, first, it is somewhat helpful to note what this Chapter in *not* about.

Whilst this chapter discusses many contentious issues in both European Union Law and the regulation of GMOs – particularly risk regulation, barriers to free trade and questions of political legitimacy to name just a few – I do not attempt to offer a rehearsal of those now well-documented debates.[1] Any references to the hotly contested issue of risk regulation are not adduced in order to offer a critique of the current system as applied to the regulation of GMOs. Rather, my concern

[1]Pollack M A and Shaffer G C, When Co-operation Fails: The International Law and Politics of Genetically Modified Organisms (Oxford University Press 2009); Maria Lee, EU Regulation of GMOs: Law and Decision Making for a New Technology (Edward Elgar 2007); in L Bodiguel and M Cardwell (eds) The Regulation of Genetically Modified Organisms: Comparative Approaches (Oxford University Press 2010).

here is to think about the suitability of the current system of regulation for regulating gene drive technologies. Some of the concerns I raise will be as true for gene drive technologies as they are for conventional GMOs. However, the suitability or otherwise of the current system for the regulation of GMOs *viz-a-viz* conventional GMOs is not my concern here.

Throughout the discussion below, talk about framing appears to range across three distinct framing debates. Firstly, what is the correct frame for understanding gene drive technologies and their regulation?

Secondly, what frames are people actually using in thinking about gene drive technologies? Thirdly, what existing frame might gene drive technologies be most easily squeezed into? The wide-ranging nature of the debate is in part symptomatic of the difficulties that we face in disentangling the mutually constitutive but different understandings of the nature of the technology, the social order that regulates it and the variety of world states these different understandings make possible. The first question is very much the enterprise of this thesis more generally. However, questions one, two and three, although distinct, oftentimes overlap. The failure to acknowledge this overlap lends existing, but yet unsuitable, frames a fixity that they do not deserve. Perhaps the best illustration of the pervasiveness and fixity of existing frames in discourses surrounding the regulation of gene drive technologies is the fact that, to date, only two suggestions have been tabled. Firstly, it has been suggested that we might regulate gene drive technologies in the same way that we regulate GMOs.

The suggestion that we regulate gene drive technologies as GMOs adopts a technical and descriptive understanding of gene drive technologies. Put simply, because gene drive technologies fall within the description ascribed to conventional GMOs, we might frame them in the same way, understanding them to be alike regulatory objects. However, unthinkingly applying this frame fails to interrogate afresh the realities and complexities of the overflows, target agents and source agents that gene drive technologies implicate. Instead, this approach presupposes that all of the overflows

generated by the deployment of gene drive technologies have been identified and managed by existing regulatory regimes.

This Chapter takes the following structure. First, I demonstrate that there is indeed a presumption within the current literature that any thinking about the regulation of gene drive technologies ought to take existing GMO regulation as its starting point. That is, there exists an assumption that conventional GMOs and gene drive technologies can be framed as identical regulatory objects. Secondly, I discuss what I call the 'background' reasons for which the frame provided by GMO regulation, in the European Union in particular, is too narrow to adequately frame gene drive technologies. This analysis largely consists of identifying those regulatory objectives that, whilst pertinent in the GMO context, are less relevant, or even irrelevant, in the context of gene drive technologies. Thirdly, I demonstrate how these background reasons and the context within which the GMO regulation emerged contributes to the omission of important concerns within the regulatory frame. This is further exacerbated by failures to take account of the distinct features of gene drive technologies as a regulatory object. These two sections taken together demonstrate that overly narrow frames come about for three reasons; problematic descriptions of the technology as regulatory objects; incompatible or sometimes irrelevant regulatory objectives; or a combination of the two.

However, when do we know that a frame is too narrow, and when does that narrowness demand framing a fresh? The second part of this Chapter adopts Roger Brownsword's taxonomy of 'Regulatory Connection' as a means of diagnosing the sorts of narrowness that demand reframing.[2] As such, I demonstrate the complementary nature of the methodology of framing and Brownsword's taxonomy of Regulatory Connection. Understanding the importance and relevance of well-constructed frames does little to help us tell good frames and bad frames apart, and so the methodology of framing provides little assistance in singling out good and bad regulatory regimes.

[2] Roger Brownsword, *Rights, Regulation and the Technological Revolution* (Oxford University Press, 2008) 160-184.

On the other hand, identifying and classifying an instance of regulatory disconnection does little to prescribe how the disconnection might be overcome. In this way, we might understand both approaches as complementary in attempts to identify inadequacies within regulatory frameworks and prescribe appropriate reforms.

1. GMOs as the Dominant Paradigm

This section demonstrates that the current literature surrounding the regulation of gene drive technologies considers existing regulations governing the production and use of GMOs to be sufficient. Here, I demonstrate that the dominant discourses concerning the legal regulation of gene drive technologies conceive of them as conventional 'green biotechnologies' and therefore falling into the same frame that we apply in the regulation of Genetically Modified Organisms. Before the existing discourses surrounding gene drive technologies are described, however, we might benefit from pausing to examine the broader field of genetic technologies more generally and how frames in this arena have been developed.

1.1 Framing of 'Green' and 'Red' Biotechnologies

Before we turn to consider contemporary discourses surrounding the use and regulation of gene drive technologies it is helpful to note the construction of two apparently distinct frames for understanding biotechnologies more generally. On the one hand there exist 'red biotechnologies', those technologies that map or alter human genomes. Generally, discussions about the regulation of 'red biotechnologies' are framed by ethical considerations – concerns about their potential implications for human nature,[3] the structure of the social order[4] and the exacerbation of inequality.[5] On the other hand, there exist 'green biotechnologies', those technologies that edit

[3] John Harris, Enhancing Evolution: The Ethical Case for Making Better People (Princeton University Press 2010).
[4] Frances Fukuyama, Our Post Human Future: Consequences of the Biotechnology Revolution (New York: Farrar, Strauss and Giroux 2002).
[5] Michael Sandel, The Case Against Perfection: Ethics in the Age of Genetic Engineering (Cambridge: Harvard University Press 2007).

plant or, less frequently, animal genomes.[6] For green biotechnologies, discussions about their regulation are framed primarily by economic and safety based considerations – concerns revolve around harm to humans and/or the environment[7] and the facilitation of free trade.[8] These two colour-coded frames are distinct with regard to the concerns they put on screen and the regulatory objectives they seek to fulfill. Up until now, there has been little cause for thinking about why and how these frames might intersect. Instead, they have been thought of as separate and perhaps even immutable. Confronted by new biotechnologies, there is a tendency to ask (consciously or otherwise) which of the two frames, red or green, the technology belongs to.

That the normative, and therefore societal and ethical features, of non-human or 'green' biotechnologies have, to date, been sidelined by discourses concerning only quantifiable risks to human health and the environment is not a novel observation. Maria Lee has noted that whilst ethical and societal considerations are foregrounded, and sometimes even take priority, in debates surrounding the permissibility of human genetic modifications or 'red biotechnologies', such considerations have sat largely outside of the frame in the context of plant and animal applications of the same technologies.[9] Furthermore, red biotechnologies have most usually been regulated by agencies with responsibility for human health. For example, pre-implantation genetic diagnosis is regulated in the United Kingdom by the Human Fertilization and Embryology Authority, an 'arms-length' body of the Department of Health.[10] Green biotechnologies on the other hand have, for the most part, been regulated by European Union norms— the regulation of GMOs being the prime example. Furthermore, the release of GMOs in the United Kingdom is regulated by the

[6] For evidence of tendency to carve up debates about the regulation of biotechnologies into colour-labelled camps see: -- in Roger Brownsword and Karen Yeung (eds) Regulating Technologies: Legal Futures, Regulatory Frames and Technological Fixes (Hart Publishing 2008).
[7] Lee (n1) 225.
[8] For just one elucidation of this understanding, see: Sara Poli, 'The Reform of the EU Legislation on GMOs: A Journey to an Unknown Destination? (2015) The European Journal of Risk Regulation 559.
[9] Maria Lee, 'Risk and Beyond: EU Regulation of Nanotechnology' (2010) European Law Review 800, 806.
[10] For an over of the history of the HFEA and its role in regulating human applications of genetic technologies, see: Emily Jackson, *Regulating Reproduction: Law, Technology and Autonomy,* (Oxford: Hart Publishing 2001). See also: <Human Fertilization and Embryology Authority https://www.hfea.gov.uk/about-us/> Last accessed 6th August 2019.

Advisory Committee on Releases into the Environment, an 'arms-length' body of the Department for the Environment, Food and Rural Affairs.[11] This chapter suggests that placing gene drive technologies within the same frame as 'green biotechnologies', and therefore failing to consider them as a distinct regulatory object, is a mistake.

To date, little has been published regarding the regulation of gene drive technologies. What has been written has, for the most part, conceived of gene drive technologies as another instance of agricultural or 'green' biotechnology and argues that it should be regulated as such. It is this trend that motivates the exploration of the suitability of the European Union's suite of genetic-modification-regulating directives below.

With regard to individual member states, the report of the Dutch Government (the only gene drive-focused report of a member state at the time of writing) suggests that the regulation of gene drive technologies ought to fall within the ambit of the GMO decrees, promulgated broadly in line with the relevant EU GMO Directives.[12] Discussions taking place at various conferences and workshops across Europe have also taken as their starting point the existing regulation concerning GMOs.

However, this trend extends far beyond European borders. The National Academies report from the United States, *Gene Drives on the Horizon,* identifies the regulation of gene drive technologies as falling under the United States Coordinated Framework for the Regulation of Biotechnology.[13] In the regulatory role that it plays, this framework is analogous to the European Union's suite of GMO Directives, insofar as its focus is the regulation of genetically engineered plants and, less often in practice, animals. The Framework delegates authority for the regulation

[11] See: Advisory Committee on Releases to the Environment, About Us https://www.gov.uk/government/organisations/advisory-committee-on-releases-to-the-environment/about Last accessed 6th August 2019.

[12] J Westra , CJB van der Vlugt, CH Roesink and PAM Hogervorst, 'Gene Drives Policy Report: RIVM Letter Report 2016-0023' https://www.rivm.nl/bibliotheek/rapporten/2016-0023.pdf Last accessed 6th March 2019.

[13] National Academies of Science, Engineering and Mathematics Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct, 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' (Washington: National Academies Press, 2016) 152.

of biotechnologies across three different agencies: US Food and Drug Administration (FDA), the US Department of Agriculture (USDA), and the US Environmental Protection Agency (EPA).

Of these three agencies, the report suggests that it is most likely that the EPA will play the major regulatory role in the development and use of gene drive technologies.[14] Conversely, the report expects the Center for Disease Control and Prevention (CDC), the United States agency with authority for public health matters, to have only an incidental role in the regulation of gene drive technologies. According to the National Academies, action on behalf of the CDC would be indicated only where the release of a gene drive threatened public health, for instance in the case of a drive that, contrary to its intended purpose, increased disease burden within the population.[15]

Thus, in the United States at least, public health agencies are conceived of as adopting only a responsive role with regard to the regulation or use of gene drive technologies, intervening only when the technology has failed to achieve its stipulated purpose, rather than having a role in developing regulations that apply *prior* to release. The report does not, therefore, conceive of gene drive as a technology that might be regulated and implemented by an agency such as the CDC as part of a broader programme aimed at improving public health. As such, we see a clear elucidation of the idea that gene drive technologies sit within the domain of green biotechnologies, framing them in the context of concerns raised by conventional gene editing technologies employed across the agricultural industry.

In the international law context, the Convention on Biological Diversity (CBD),[16] and the Cartagena Protocol in particular, [17] have been identified as the relevant international agreements regulating the use of gene drive technologies by a range of international reports and documents.[18] Given that the Cartagena Protocol is *the* international agreement regulating the risks posed by GMOs it seems that, like domestic arrangements, the international arena also considers gene drive

[14] Ibid 152.
[15] Ibid 152.
[16] United Nations, Convention on Biological Diversity (1992).
[17] Cartagena Protocol on Biosafety to the Convention on Biological Diversity (2000).
[18] National Academies of Science, Engineering and Mathematics (n13).

akin to conventional green biotechnologies. Twice since 2015, the CBD has convened meetings to debate a moratorium on gene drive research, once at the Conference of the Parties to the Convention in 2016 and a second time at the Conference of the Parties in Egypt in 2018.[19] As such, it is clear that both the CBD itself, as well as its member state signatories, have recognised the Convention's authority in matters concerning the regulation of gene drive technologies.[20]

Having reviewed the current consensus regarding the regulation of gene drive technologies, it becomes clear that most, if not all, of the domestic, supra-national and international legal instruments, which various commentators suggest ought to be applied, are drawn up in accordance with thinking around the regulation of GMOs. In this way, it is clear that current thinking about the regulation of gene drive technologies is dominated by frames borrowed from the conventional GMO paradigm. This is because gene drive technologies as regulatory objects have, up until now, been identified as analogous to conventional agricultural biotechnologies. This is problematic for a number of reasons. In the first instance, the suitability of the current framework with regard to regulating its intended regulatory target (GMOs) is questionable, although not our concern here. Secondly, failing to frame gene drive technologies as a distinct regulatory object raises a range of serious concerns discussed below.

2. The Context of European Union GMO Regulations

In order to properly articulate the objectives of the European Union's regulation of GMOs, it is important to understand the context within which the regulation emerged. Only in understanding these features can we properly see how the contours of the frame encircling the regulation of

[19] In 2016 see: Ewen Callaway, "Gene Drive' Moratorium shot down at UN Biodiversity Meeting' (21st December 2016) Nature https://www.nature.com/news/gene-drive-moratorium-shot-down-at-un-biodiversity-meeting-1.21216 Last accessed Monday 25th March 2019. In 2018 see: Ewen Callaway, 'UN Treaty Agrees to Limit Gene Drives but Rejects a Moratorium' (Nature 29th November 2018). https://www.nature.com/articles/d41586-018-07600-w. Last accessed Monday 25th March 2019.

[20] The Cartagena Protocol is one of a number of different international agreements that are likely to be applied to the regulation of gene drives technologies. It is however, to date, the only one that has been recognised explicitly by the international community. The SPS Agreement, the Aarhus Convention and the Nagoya Protocol are all relevant to the international regulation of GMOs and, for that reason, might also find some applicability in the gene drive context (if the international community continue to conceive of gene drive technologies as conventional agricultural biotechnologies).

GMOs came to be drawn and the ways in which they are too narrow for the regulation of gene drive technologies. In this section, we come to understand how certain regulatory objectives (particularly those of quantification and control described below) came to dominate the framing of genetically modified organisms and their proper regulation. Whilst reliance on technical expertise is commonplace in areas of high technological complexity, we see this tendency further exacerbated in the GMO context by political challenge and the particularities of the legal culture of the time. Furthermore, we note the ways in which these regulatory objectives appear to be at odds with the proper regulation of gene drive technologies. Broadly speaking, we consider three factors contributing to a system of regulation framed by a desire for quantification and control of risk.

The tail end of the 1990s, the time during which the regulation of GMOs was being promulgated in the European Union, can be characterised as an era of flux for the European Union institutions responsible for developing policy on these issues. What resulted from the particular cultural and political milieu of the period was a body of regulation concerned with the quantification and control of risk. Of the cultural and political milieu, three factors have been identified as significant. In the first instance, we consider the relevance of the BSE outbreak of the late 1980s/early 1990's and the identification of the link with the human form of the disease – vCJD. Secondly, we consider the influence of transatlantic policy – particularly the approach adopted in the United States Coordinated Framework on Biotechnology.[21] In this connection, we also note concerns for free movement of goods within the internal market and the effect of the WTO SPS agreement.[22] Finally, we discuss the waning confidence in the political legitimacy of the European Commission. The relevance of each of the factors will be examined, albeit briefly, in turn.

[21] Co-ordinated Framework on Biotechnology 1996 (United States of America).
[22] The Agreement on the Application of Sanitary and Phytosanitary Measures (15 April 1994) LT/UR/A-1A/2 art 2. Available at https://www.wto.org/english/docs_e/legal_e/15sps_01_e.htm Last accessed 6th August 2019.

2.1 The Relevance of the BSE Crisis

In 1996, the British Government announced a link between Bovine Spongiform Encephalopathy (BSE) – a prion disease that had been recorded in cattle since the mid-1980s – and the human form of the disease, vCJD.[23] The cause of BSE in cattle was attributable to feeding calves on meat and bone meal mixtures in an attempt to save costs on grain and therefore produce beef more cheaply than ever before.

That regulators had failed to identify and prevent the harms arising from moving beef cattle to a carnivorous diet from an herbivorous one became a serious cause for public concern. The notion that policy and regulation surrounding agricultural practices within Europe had been so inadequate as to cause the creation of a terminal neurological disease, became a highly resonant theme in public discourse.[24]

Mark Pollack and Gregory Shaffer draw an explicit link between the BSE crisis and the character of the GMO regulations of the late 1990s, noting that, 'the implementation of the new regulations quickly became inextricably and controversially linked to a series of food-safety scandals that rocked the Union during the second half of the 1990s, most notably the BSE scandal that struck in 1996'.[25] The BSE scandal induced a duality of mistrust in publics, diminishing confidence in the reliability of scientific advice[26] and reducing trust in regulators to make decisions about risk.[27]

It was in the context of heightened public concern regarding food safety and the regulation of risk that GMOs burst onto the scene. Maria Weimer notes that the overall effect of the BSE

[23] *Hansard*, HC Deb, vol 275, col 375 (20 March 1996); For a complete record of the BSE crisis and an overview of the way in which it unravelled see: Phillips Report, *Inquiry into the emergence and identification of Bovine Spongiform Encephalopathy (BSE) and variant Creutzfeldt-Jakob Disease (vCJD) and the action taken in response to it up to 20 March 1996* (House of Commons, 2000) http://www.bseinquiry.gov.uk/ Last Accessed Tuesday 30th July 2019.
[24] Kevin E. Jones, 'BSE, risk and the communication of uncertainty: A review of Lord Phillips' report from the BSE inquiry (UK)', Canadian Journal of Sociology 26(4) (2003), 655-6.
[25] Pollack and Shaffer, (n1) 64.
[26] Sheila Jasanoff, 'Civilization and madness: The great BSE scare of 1996', Public Understanding of Science 6 (1997), 221-32.
[27] Graham R. Chambers, 'The BSE Crisis and the European Parliament' in Christian Joerges and Ellen Vos (eds), *EU Committees: Social Regulation, Law and Politics* (Hart Publishing, 1999).

scandal on GMO regulation was to create a system of regulation that was constitutionally committed to high levels of public health and environmental protection in the internal market and one that was self-conscious about the manner in which it went about fulfilling those commitments.[28] As such, there developed an increased emphasis on objective risk assessment that left little room for discretionary decision-making on behalf of public officials. This, in turn, helped to justify the Control Model of regulation characteristic of the GMO legislation of the period discussed below.

2.2 Influence of Transatlantic Policy and the WTO

The second contextual factor affecting the European Union's approach to the regulation of GMOs is the influence of transatlantic GMO policy, as well as the jurisprudence of the WTO – particularly with regard to the Sanitary and Phytosanitary Measures Agreement.[29]

During the European Union's *de facto* moratorium on the authorization of GMOs, the Bush Administration became increasingly concerned with preventing the proliferation of the EU's precautionary approach into other States for fears that trade might be adversely affected.[30] This concern became ever the more pressing when a number of African States, including both Mali and Burkina Faso, adopted legislation regulating GMOs based in no small part on the European Union's precautionary model.[31] This in part, motivated the United States' decision to lodge a complaint with the Appellate Body of the WTO with regard to the trade barriers flowing from the European Union's *de facto* moratorium. As Pollack and Shaffer put it, the United States hoped that with a little pressure from the WTO the European Union's regulatory approach could be reoriented, away from precautionary principles and towards hard science.[32]

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[28] Maria Weimar, *Risk Regulation in the Internal Market: Lessons from Agricultural Biotechnologies* (Oxford University Press, 2019) 89-90.

[29] The Agreement on the Application of Sanitary and Phytosanitary Measures (15 April 1994) LT/UR/A-1A/2 art 2. Available at https://www.wto.org/english/docs_e/legal_e/15sps_01_e.htm Last accessed 6th August 2019.

[30] Mark A Pollack, 'International Trade and Risk Regulation: Whatever Happened to the Transatlantic GMO Conflict?' (2013) American Political Science Association 2013 Annual Meeting https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2299609 Last accessed 6th August 2019.

[31] See: Law n° 064-2012/an, - *establishing a regime of safety regulations in the area of biotechnology*. [Burkina Faso]; Loi n°08-042/an, – *rm du 1er decembre 2008 relative à la sécurité en biotechnologie en république du mali. l'assemblee nationale.* [Mali]

[32] Shaffer and Pollack (n1).

The final decision of the WTO with regard to the complaint was finally published in 2006 – two years after the nominal end of the *de facto* moratorium and three years after the implementation of the new suite of legislation governing the use and release of GMOs in Europe.[33] However, as a number of scholars have noted, it is hard to overstate the role that this ongoing legal battle had in shaping the European Union's reform of its post-moratorium GMO regulation. An understanding of the very broad applicability of the SPS Agreement in the GMO arena (as was confirmed in the EC-Biotech decision) [34] pushed the Union toward a model of regulation driven by scientific advice and assessment. As Maria Lee notes, the sovereignty of science in decision-making under the SPS Agreement is, effectively, unimpeachable.[35] Disruptions to trade, according to the SPS, can only be justified by reference to new scientific evidence, not evolving social or political understandings of a problem, not emerging questions about the acceptability and suitability of the scientific method for gathering the relevant information, not social or political change. This approach to decision-making under the SPS is not particular to the regulation of GMOs alone – elsewhere Joanne Scott has described the WTO's approach to science as open 'to charges of epistemological imperialism, and positivistic simple-mindedness'.[36] In this way, the SPS agreement itself understands and relies on technical expertise before anything and has itself come to be understood in technical terms.[37] Despite this, however, the effect of the SPS's positivistic approach on the regulation of GMOs in Europe should not be understated.

In this way, then, if the European Union was to fulfil its obligations under various international agreements, it needed to demonstrate a willingness to adopt the top-down, scientifically determined approach to decision-making around GMOs favoured under the WTO

[33] Council Directive 2009/41/EC of 6 May 2009 on the contained use of genetically modified micro-organisms OJ L125/75; Council Directive 2001/18/EC of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC OJ L106/1 [hereafter "Directive 2001/18/EC"]

[34] DS291:European Communities – Measures Affecting the Approval and Marketing of Biotech Product https://www.wto.org/english/tratop_e/dispu_e/cases_e/ds292_e.htm Last accessed 6th August 2019.

[35] Lee (n1) 225.

[36] Joanne Scott, The WTO Agreement on Sanitary and Phytosanitary Measures: A Commentary (Oxford University Press 2009) 3.

[37] Elizabeth Fisher, Risk Regulation and Administrative Constitutionalism (Hart Publishing 2007) Chapters 5 & 6.

and by the United States. As such, Pollack and Shaffer have noted the ways in which both US practice and WTO jurisprudence have been incorporated into the post-moratorium framework – most obviously in the establishment of EFSA.[38]

2.3 Waning Confidence in the Political Legitimacy of European Union Institutions

Confidence in the political legitimacy of the European Community Institutions – and the Commission in particular, had receded considerably by the end of the 1990s. In part, this was attributable to the *Report of the Committee of Independent Experts* making findings of fraud and extensive mismanagement across the range of Commission responsibilities, but with regard to agricultural policy particularly.[39] The publication of the Report led to the immediate and *en masse* resignation of all members of Jaques Santer's Commission. As Paul Craig notes, this dramatic turn of the events became the focus of both reputable, and less reputable, newspapers across Europe for some time.[40] As such, decision making surrounding the regulation of the GMOs during the *de facto* moratorium took place under a caretaker Commission headed by Manuel Marin and at a time during which the legitimacy of EU institutions was seen to be hanging by a thread.

However, institutional misfeasance was not the only cause for concern with regard to the legitimacy of the European Union project of integration. The BSE crisis mentioned above played a significant role in reducing public confidence in decisions made at the supranational level.[41] Furthermore, it was during this period that fears that the European project was to be, by its nature, dogged by a 'democratic deficit', began to crystalize.[42]

In the face of waning public confidence and ebbing political legitimacy, the Commission sought to promote a sense that Commission decision-making could and would be held

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[38] Pollack and Shaffer (n26) 24.
[39] Committee of Independent Experts, First Report on Allegations regarding Fraud, Mismanagement and Nepotism in the European Commission (15 March 1999), para 1.4.2.
[40] Paul Craig, 'The Renewal and the Fall of the Commission: Accountability, Contract and Administrative Organization' (2000) European Law Journal 98, 99.
[41] Chambers (n27).
[42] J Weiler, *The Constitution of Europe: Do the New Clothes Have an Emperor? (*Cambridge: Cambridge University Press 1999).

accountable. It was this need to promote the Commission's accountability that Liz Fisher suggests, at least in part, motivated the Commission to publish its Communication elucidating how the Precautionary Principle would be applied.[43] Aside from this clarification of one of the Union's guiding regulatory norms, we might also link the Commission's desire to demonstrate its accountability and transparency with what became a 'top-down' system of quantification and control, with regard to conceptualizing and managing the risks associated with GMOs.

2.4 The Context and Its Consequences for Framing

The need to promote accountability, build perceptions of political legitimacy, and facilitate free trade within the Union and barrierless trade beyond drives toward a particular model of decision-making in areas of technological risk. Liz Fisher describes the governance reflected by the GMO regulation as one belonging to the 'Rational-Instrumental paradigm' of decision-making,[44] whilst Maria Weimar has recently described it as a Control Model of regulation.[45]

However, labels aside, for our purposes the pictures drawn by both scholars are quite the same with regard to the regulation of GMOs. The Rational-Instrumental paradigm describes a mode of decision-making dominated by a reliance on objectivity, the analytical methodologies of experts, and the subordination of discretion to scientific measurements and thresholds.[46] Within the Rational-Instrumental paradigm, risks are scientifically or economically quantifiable and the implications of scientific uncertainty can be reduced to irrelevance by rational, science informed and expert led methodologies.

Similarly, Weimar's description of the Control Model of public administration portrays a system within which decisions to grant or withhold authorization are dominated by scientific advice, squeezing out the need for discretionary judgment on behalf of the Commission. The

[43] Elizabeth Fisher, 'Opening Pandora's Box: Contextualizing the Precautionary Principle in the European Union' in Michelle Everson and Ellen Vos (eds) *Uncertain Risks Regulated* (Routledge 2009).
[44] Fisher, (n37) 28-30.
[45] Weimar, (n28) 116-119.
[46] Fisher (n37) 29.

Control Model understands risks as quantifiable and measurable, scientific uncertainty as eliminable and knowledge as 'an objective body of truth claims based on established facts'.[47]

As such, both the Rational-Instrumental paradigm and the Control Model of public administration seek to subject matters of high technological complexity to frames of quantification and control as a means of overcoming concerns for political legitimacy and *ex poste* accountability. In this way, then, we can begin to account for the narrowness of those frames constructed in the regulation of GMOs in Europe.

Heavy reliance on scientific advice and quantifiable scientific measurements restricts the range of knowledge claims admissible within the context of regulatory decision-making. This is not to say that these knowledge claims are not useful in and of themselves, but rather the knowledge claims rendered by experts with scientific, analytical methodologies do not avail decision-makers of the full picture. Beyond the narrow contours of knowledge claims that might be subjected to the quantification and measurement that make *ex poste* accountability possible, lie a range of important knowledge claims that cannot be so easily subjected to actuarial evaluation. Furthermore, reliance on objectivity and quantification preclude certain experts from the decision-making process, because expertise and knowledge claims that cannot be counted or calibrated are, to some extent at least, tantamount to the exercise of accountability-defeating discretion. The relevant knowledge claims that lie beyond calculable range are potentially innumerable, but they do include claims about the ethical quality of technology and its regulation, claims regarding the social or cultural impacts of the technology and claims surrounding the effects of human behaviour on risk.

The previous Chapter outlined the range of overflows that the regulation of gene drive technologies ought to take into account as a part of the framing process. It takes little imagination

[47] Weimar (n28) 118.

to understand the ways in which reliance on quantification and control obscure the discovery of these overflows.

However, the contextual factors described above that were so influential in the framing of both GMOs as a regulatory object and their proper regulation are notably absent from questions surrounding the regulation of gene drive technologies. In the context of gene drive technologies, there need be little concern for compliance with WTO obligations, crises of political legitimacy and the particular understandings of science that they invite. As such, before we move on to think about the particular understanding of gene drive as a regulatory object that such a framework reflects, there are freestanding reasons for rejecting a frame built in response to a particular, and largely irrelevant, cultural context.

3. Describing Gene Drives as a Regulatory Object

Whilst what went above considers the ways in which cultural and political contexts might lead to the development of overly narrow frames for an understanding of a technology, this section considers challenges flowing from inaccurate descriptions of a technology as a regulatory object. Put simply, this section describes the problems that we encounter if we try to treat gene drives as a regulatory object akin to those regulated as GMOs. As such, the aim of this chapter is to describe the reasons for which gene drive technologies ought not be considered an analogue of conventional GMOs.

Although the structure of this Chapter invites the suggestion that we might consider political context and problematic descriptions of regulatory objects as distinct influences on the construction of frames, that is not the case. In fact, in many cases the interactions between the political aspirations of a body of regulation and the ways in which that regulation describes its regulatory target do much to reinforce the narrowness of the frame constructed. For example, the GMO regulations are overly narrow because they fail to incorporate a range of gene drives that are built without using techniques or methods of genetic modification described in the Regulation. As is highlighted below, so called *Wolbachia* gene drives sit outside of the purview of existing

regulation because they are not created using conventional gene editing techniques. In this context, the narrowness of the existing frame is the product of both a problematic description of gene drive as a regulatory object and the particular political commitments of the GMO regime. Current attempts to bring gene drive technologies under the umbrella of conventional GMOs presuppose a certain description of gene drive technologies as a regulatory object, in short, that they are sufficiently similar to GMOs for the purposes regulation to be treated alike.

However, the GMO/non-GMO boundary is so resonant and hotly contested because of the regulation's commitments and objectives – ensuring the free movement of goods in particular. Because an organism's status as GM or non-GM product has particular implications for trade, discerning whether an organism is the product of genetic modification becomes a profoundly important question orientating the regulatory response. Whilst these characteristics were crucial to understanding GMOs as regulatory objects, they are of little to no relevance to the ways in which we understand gene drive technologies. In understanding the interaction between chosen descriptions of a regulatory object and the political, social or economic aspirations or regulatory objectives, we can begin to understand the myriad ways in which overly narrow frames come to be built.

3.1 GMO Regulation in Europe

The discussion above charted the cultural and political context within which the European Union's post-moratorium framework for GMO regulation was drawn up. This section takes the time to describe precisely what that framework of regulation looks like. This is important given that it is this body of regulation that is currently thought to regulate the use of gene drive technologies. The description of the regulation offered below highlights the emphasis on quantification and control of risk as it appears throughout the legislation itself. In this way, we can point, in a concrete fashion, to the manner in which the political, social and economic milieu of the era, alongside inaccurate descriptions of gene drive technologies as a regulatory object, both translate directly into an overly narrow range of regulatory frame.

3.1.1 Contained Use Directive

While Directive 2009/41/EC on contained use only applies to Genetically Modified Micro-Organisms (GMMs), the domestic Contained Use Regulations extend regulation to larger genetically modified organisms, thus encompassing both GMOs and GMMs, with gene drives falling into the former category.[48] Article 4(2) of Directive 2009/41/EC mandates the performance of a risk assessment to ascertain the risks to human health and the environment of the proposed activity. The risk assessment should, at minimum: identify any harmful effects, describe characteristics of the activity, and evaluate the severity and likelihood of the potentially harmful effects.[49] Article 4(3) of the Directive then specifies a system for classifying GMOs in accordance with their attendant risks, largely on the basis of potential pathogenicity.[50] There are four possible classifications, which are gradated in accordance with the perceived level of hazard: Class 1 (activities of no or negligible risk); Class 2 (activities of low risk); Class 3 (activities of moderate risk); and Class 4 (activities of high risk).[51] Once a GMO has been classified for the purposes of the Directive, the necessary containment level is imposed for the protection of human health and the environment. For the most part, the potentially harmful effects envisaged by the risk assessment procedure are limited to clinically or economically quantifiable harms.

There are four containment levels, corresponding to the risk classifications specified by Article 4(3) (further details of containment measures can be found in Annex IV of the Directive). Where a premises is to engage in the contained use of GMOs for the first time, those proposing the activity must submit prior notification to the competent authorities. In the United Kingdom, the Health and Safety Executive, in conjunction with the Secretary of State for the Environment, Food and Rural Affairs (Defra), fulfil the role of the competent authority.[52] The rigour of the

[48] Health & Safety Executive, 'The Genetically Modified Organisms (Contained Use) Regulations 2014: Guidance on Regulations' (Health & Safety Executive, London 2014) 5.
[49]Council Directive 2009/41/EC (n33), Annex III.
[50] Ibid Art 4(3).
[51] Ibid Art 4(3).
[52] Health & Safety Executive, 'The Genetically Modified Organisms (Contained Use) Regulations 2014: Guidance on Regulations' (Health & Safety Executive, London 2014) 5.

notification process escalates from Class 1 to Class 4 and, whilst consent for the proposed activity can be withheld by the competent authority, such action is largely restricted to Class 3 and Class 4 activities. Further, as has been noted elsewhere, barring the ability to grant or withhold consent following notification, the role of the competent authority is limited.[53] With regard to the domestic implementation of Directive 2009/41/EC, extensive guidance has been provided by the Scientific Advisory Committee on Genetic Modification (SACGM).[54]

3.1.2 Deliberate Release Directive

In accordance with Article 4(2) Directive 2001/18/EC, those intending to release genetically modified organisms must perform an environmental risk assessment, as outlined in Annex III. Following risk assessment, those who intend to release GMOs into the environment must notify the competent authority in accordance with Article 6(1).

This notification procedure requires: the submission of a technical dossier supplying the information specified in Annex III necessary for carrying out the environmental risk assessment of the deliberate release of a GMO or a combination of GMOs; the completed environmental risk assessment; the conclusions required by Annex II, Section D; and any bibliographic reference and indications of the methods used.[55] This dossier will comprise information including: the conditions of release and the potential receiving environment; interactions between the GMO and the environment; emergency response plans; waste treatment plans and control plans. With regard to framing, the 'overflows' that ought to be considered relevant as part of the authorization process are prescribed by the terms of the technical dossier, limited to quantifiable environmental risks. The reliance on scientifically or economically measurable harms is unsurprising given the need to reduce the margin of discretion within which authorization decisions are made.

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[53] Marianne Friant-Perrot, 'The European Union Regulatory Regime for Genetically Modified Organisms and its Integration into Community Food Law and Policy' in Luc Bodiguel and Michael Cardwell (eds), *The Regulation of Genetically Modified Organisms: Comparative Approaches* (Oxford University Press 2010) 83.
[54] Health and Safety Executive, 'The SACGM Compendium of Guidance' (Health and Safety Executive, London 2006).
[55] Council Directive 2001/18/EC, (n33) Art 6(2).

Once a notification has been submitted, it is for the competent authority (in the United Kingdom's case the Health and Safety Executive and Defra) to examine the application and consider any observations made by other Member States through the Article 11 exchange of information procedure.[56] The competent authority must either authorize or reject the application for release within 90 days of the notification.[57]

The legal detail of the regulatory regime described above is one that bears out the description of the regulation laid out in Section Two. Decision-making under the GMO Directives relies on scientific evidence and advice, characteristic of the conception of science developed by rational-instrumental or control models of regulation. Not only is this demonstrated by virtue of the particular risks accounted for in the prescribed risk assessment (quantifiable risks to human health and the environment), but also by the institutional character of the agencies evaluating those risk assessments. For instance, in the United Kingdom, ACRE – the committee responsible for reviewing risk assessments and authorizing (or refusing to authorize) – consists of scientists alone. In this way, we see the institutional separation of science from other domains of decision making. This institutional arrangement is reminiscent of what Liz Fisher has called the 'kettling of science' and is a further demonstration of a particular understanding of science in law and policy and one that privileges approaches of technological determinism in order to avoid concerns regarding a usurpation of democracy.[58] Furthermore, the overflows that the regulation focuses on (and those with which the scientists are charged with assessing) are only those overflows discoverable by analytical processes – quantifiable measures of pathogenicity, environmental persistence and physical harm.

[56] Ibid Art 6(5), Art 11.
[57] Ibid Art 6(5).
[58] Elizabeth Fisher, 'Sciences, Environmental Law and Legal Cultures: Fostering Collective Epistemic Responsibility' in Emma Lees and Jorge E Viñuales (eds) *The Oxford Handbook of Comparative Environmental Law* (Oxford: Oxford University Press: 2019).

4. The Unsuitability of GMO Regulations for the Regulation of Gene Drive Technologies

Having considered the social, political and cultural context surrounding the regulation of GMOs in Europe, this Section focuses on a range of concrete examples of the ways in which the regulation of GMOs presents an overly narrow frame from which discussions regarding the regulation of gene drive technologies might be developed.

4.1 Risk Regulation

In legal analyses of the regulation of GMOs, the most ink has been spilt in criticising the European Union's approach to risk. Numerous volumes discuss the problematic application of the precautionary principle and its detrimental effects on agriculture, biotechnology and innovation.[59] However, if the framework is problematic for the regulation of genetically-modified crops and feed, it is nonsensical as applied to gene drive technologies. The difficulties surrounding certain conceptions of science and the implications that they have for the ways in which we construct technological frames are perhaps most profound in the context of risk regulation.

The concerns here are two-fold. In the first instance, I suggest that reliance on comparison with 'conventional counterparts' is problematic insofar as it represents a confused understanding of the salient features of gene drive technologies – both in terms of the purposes for which they might be used, and their metaphysical properties. In the second instance, I suggest that a failure to engage with the benefits of gene drive technologies as a part of the risk assessment process represents another failure in attempts to describe gene drive technologies as a regulatory object.

4.1.1 Understanding 'Conventional Counterpart'

The risk assessment mandated by Article 6 of the Deliberate Release Directive requires risk assessors to compare the risks associated with the GM construct to the risks associated with the non-modified organism, or what is referred to as the 'conventional counterpart'.[60] A literal

[59] Fisher (37); Liz Fisher, 'Opening Pandora's Box: Contextualising the Precautionary Principle in the European Union' in Vos and Everson (eds) *Uncertain Risks Regulated* (Routledge 2009).
[60] Council Directive 2001/18/EC, (n33) Art 6.

interpretation of Article 6 as it is applied in the crop context requires risk assessors to compare the risks associated with one means of crop cultivation with the risks associated with another means of crop cultivation, i.e., traditional breeding techniques versus GM techniques.

Taking the same approach in the context of gene drive technologies makes little, if any sense at all. A literal interpretation of the risk assessment required by Annex II would require risk assessors to compare the risks of a gene drive mosquito with the risks posed by the non-modified mosquito. As such, risk assessors would be comparing the risks associated with a means of insect control to the 'risks' associated with a wild-type mosquito. Not only is this a case of comparing apples and pears, but one that draws on the notion of established tolerable risks.

In the crop context, we are measuring the risks of the new organism (the GM crop) against the orthodoxy – an organism whose risks have been measured and considered tolerable. This approach is to be expected given the description of the Rational-Instrumental paradigm of regulation described in Section Three above. The regulation seeks to compare two phenomena, both of which it considers amenable to data collection, quantification and control.

The EFSA guidance on the risk assessment of GMOs, published in 2006, explicitly roots the rationale for the comparative assessment in the 'underlying assumption that traditionally cultivated crops have gained a history of safe use for the normal consumer or animal and the environment. These crops can serve as a baseline for the environmental and food/feed safety assessment of GMOs.'[61] This guidance, and the rationale it reflects, is in part an artefact of the European Union's near exclusive focus on crops and plant-based organisms in the GM context. Such a focus is hardly surprising given the historical and contemporary role of agriculture in polity building, but it is problematic for our purposes in a number of ways, the current objection being just one.[62] For gene drive technologies, it makes little sense to describe the wild type mosquito as

[61] European Food Safety Authority, 'Guidance Document Of The Scientific Panel On Genetically Modified Organisms For The Risk Assessment Of Genetically Modified Plants And Derived Food And Feed' (2006) 99 *The EFSA Journal.*

[62] Maria Lee, *EU Regulation of GMOs: Law and Decision Making for New Technologies* (Elgar 2009) 61.

an organism presenting an established and tolerated risk or providing an acceptable baseline for comparison; communities use insecticides, bed nets and larval traps to *reduce* wild type mosquito populations – the very same function that gene drive technologies are seeking to fulfil.

Despite our criticisms of the literal interpretation of risk assessment procedure mandated by Article 6, a shift towards a purposive interpretation is unlikely to resolve the issue. Engaging in a purposive interpretation, and thus one that identifies the correct analogue for 'crop cultivation', suggests that the risks of gene drive insects should be compared to the risks of other methods of insect control. In that case, our conventional counterpart is other methods of insect control rather than the wild type mosquito, and encompasses measures such as insecticide spraying, bed nets, larval traps and classical biological control. Indeed, it is this sort of purposivism that, as mentioned above, leads some to suggest that gene drive technologies ought to be regulated under the auspices of legislation concerning the use of pesticides and insecticides.

However, such an approach still leads to the prohibition of a gene drive release as, within the European Union, 'conventional counterpart' is considered an idealised, zero-risk alternative to the proposed action. Consequently, in assessing new technologies, unless it can be demonstrated that the proposed activity poses zero risk of adverse effects, authorisation for deliberate release will be denied. As such, a release of gene drive organisms would be prohibited before a more apt assessment of the technology's risks could be pursued. In this way, we see that the frame applied is too narrow to incorporate all of the relevant knowledge claims.

The European Union is not the only jurisdiction to engage in a comparison of conventional counterparts when assessing risk. Regulations in several jurisdictions, including the United States[63] and Brazil,[64] also draw upon this notion of equivalence in their domestic approaches to the risk evaluation of GM products. However, whilst in theory the approaches of these jurisdictions appear

[63] Coordinated Framework for the Regulation of Biotechnology https://www.aphis.usda.gov/brs/fedregister/coordinated_framework.pdf Last Accessed 21st September 2016; National Environmental Policy Act 1960.
[64] Normative Resolution No. 5 of March 12th 2008, Annex IV (Brazil).

alike, their application in practice remains quite different. Applications for the release of GM insects (note, here we are referring to non-gene drive but comparable organisms) have been reviewed and approved in both the US and Brazil.[65] The same is not true in the European Union, where an application for the release of the GM Spanish Olive Fly was withdrawn by Oxitec, the company seeking permission for the insect's release.[66] Oxitec withdrew the application when they found that the costs of conducting the research necessary to provide the competent authority with the requested risk data was too costly.[67]

There is no single reason for these different outcomes, but the existence of additional legal measures in the United States, and a culture of GMO exceptionalism in the European Union, both seem likely candidates. Indeed, recalling Jasanoff, the idiom of co-production and the idea that science and social orders are mutually constituted goes someway to explain divergent approaches to the same regulatory objects that present across different cultures.[68]

Furthermore, the divergence in legal culture leads to divergence in legal detail. For example, in the United States, Section 102(C)(iii) of the National Environmental Policy Act 1969 mandates the consideration of the 'no action alternative' to the proposed course of action, and an assessment of its impacts. This additional legal requirement plays a significant role in expanding the range of world states that we consider relevant when assessing the technologies. In most cases, and in the case of GM insects particularly, this alternative serves as a proxy for engaging in a thorough assessment of the impacts of the status quo. In this way then, the *status quo* – or the desirability of the current world states – becomes a relevant feature in terms of framing the regulatory object.

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[65] FDA, 'Environmental Assessment for Investigational Use of *Aedes aegypti* OX513A' see: <https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm490246.html> Last Accessed 4th May 2017; CTNBio, 'Technical Report 3964-2014 on the Commercial Release of Strain OX513A of *Aedes Aegypti* Process 01200.002919-2013-77' http://ctnbio.mcti.gov.br/documents/566529/686098/Thecnical+Report+3964-2014+-+-+Commercial+Release+of+strain+OX513A+of+Aedes+aegypti+-+Process+01200.002919-2013-77/be405f52-a1a5-4c01-97a6-5cd95e058e53 Last Accessed 10th May 2017.

[66] -- 'Olive Fly' (Oxitec, July 2016) http://www.oxitec.com/agriculture/our-products/olive-fly/ Last accessed 10th May 2017.

[67] Ibid.

[68] Sheila Jasanoff, 'The Idiom of Co-Production' in Shelia Jasanoff (ed) *States of Knowledge: The Co-Production of Science and Social Order* (Routledge 2004) 3.

Whilst the divergent approaches of the United States and the European Union with regard to regulation of GMOs serves as a good example of what we might call 'co-production in practice', it also serves as an illustration of the choices that we can make in the framing of new technologies. Including or excluding certain analyses (in this example, an analysis of the desirability of the *status quo*) plays a significant role in conditioning our understanding of the phenomena in question and its place in the world.

In the FDAs final assessment of the environmental release of Oxitec's OX513A mosquito, a discussion of the 'no action alternative' to the insect release is provided at some length.[69] This discussion details the current insect control methods (such as insecticide spraying and larval traps) that would continue to be used if a release of OX513A were to be denied, as well as the impact such methods have on the human environment. Further, the discussion also considers the efficacy of the current insect control techniques and the public health implications of failing to manage mosquito populations effectively. In this way, the risks of the GM insect are compared to the *actual* risks associated with the current alternative, where the current alternative is also the conventional counterpart.[70]

In addition to these legal differences, the influence of political and cultural differences is hard to overstate. One does not have to venture too far into the literature concerning the regulation of GMOs before being confronted with descriptions of the GMO exceptionalism so prevalent in Europe.[71] This exceptionalism, in combination with the application of the Precautionary Principle as explicitly mandated by the Deliberate Release Directive, has a significant impact on the assessment of risks associated with GMOs. Maria Lee suggests that we might perceive the European Union approach to regulating GMOs as one precluding the authorisation of organisms

[69] Environmental Assessment for Investigational Use of *Aedes aegypti* OX513A, 18-21.
[70] Further, in taking into account the public health implications of failing to implement the proposed technology, the "no action" alternative assessment also captures elements of the benefit of the proposed technology. This issue will be returned shortly.
[71] For particularly insightful accounts see: David Vogel, *The Politics of Precaution: Regulating Health, Safety, and Environmental Risks in Europe and the United States* (Princeton University Press 2012); Han Somsen, 'GMO regulation in the Netherlands: a Story of Hope, Fear and the Limits of 'Poldering' in Everson and Vos (eds) *Uncertain Risks Regulated* (Routledge 2009).

that pose *any* adverse effects.[72] Whilst such a position might appear extreme, it is, I argue, supported by the evidence we have of decision making in Europe and the United States and the associated legal and political causes. Once we consider that the European Union system denies an assessment of a 'no action alternative' and its risks, engages in a stringent application of the precautionary principle and operates in a political context of GMO exceptionalism, a picture emerges of a tendency to perceive the conventional counterpart as an idealised, zero-risk alternative and the proposed activity as presumptively worse.

Relying on an analysis of comparison with an already existing 'conventional counterpart' plays a significant role in the framing of gene drive technologies as a regulatory object. At least in part, this is because such an approach requires us to confine thinking to comparison with existing technologies or practices. In essence, it requires us to ask how gene drive technologies are similar to phenomena we consider ourselves to have a good understanding of, whilst disregarding the differences between gene drive technologies and the regulatory object we choose as the 'conventional counterpart'. In terms of developing a frame capable of accommodating all of the overflows that gene drive technologies produce, this approach is problematic insofar as it requires an assessment of the relative magnitude of a certain type of overflow generated by the conventional counterpart, rather than the range of actual overflows gene drive technologies might create.

4.2 Lack of Risk/Benefit Analysis

These interpretative difficulties lead to a broader criticism of the GM framework, and one that is pivotal in the gene drive context: the lack of risk/benefit analysis. Risk/benefit analysis of genetically modified organisms has been used by both New Zealand[73] and Australia[74] for over a decade. In the United Kingdom, this approach to risk evaluation has recently been advocated for

[72] Maria Lee, 'Beyond Safety? The Broadening Scope of Risk Regulation', Current Legal Problems, 62 (2009), 242.
[73] Biosecurity Act 1993 (New Zealand); Hazardous Substances and New Organisms Act 1996 (New Zealand).
[74] Gene Technology Act 2000 (Australia).

GM Insects by the House of Lords,[75] the British Ecological Society,[76] Rothamsted Research,[77] The Pirbright Institute,[78] the Wellcome Trust[79] and ACRE.[80] For gene drive technologies, which can provide public health and conservation benefits on a scale not previously achievable, the ability to consider benefit is particularly pertinent and an important aspect of the way in which we might broaden the framing of gene drive technologies.

The existing legislative framework precludes any assessment of these benefits when deciding whether a product should be authorised. Given that the risks of gene drive organisms for the control of vector-borne disease are higher than conventional counterparts (i.e. they are self-sustaining and potentially irreversible, to name just two), this is a serious point of concern.

Gene drive technologies pose several risks, some certain, others uncertain and others unknown. As such, gathering more data regarding the effects of gene drive technologies on the local and global ecology, the environment and human health is essential. Phased testing programmes have been developed for other GMOs to reduce and manage risk during the collection of this data.[81] As such, risk reduction strategies implemented throughout phased testing play a key role in increasing confidence in, and the acceptability of, the technology from a risk perspective. With respect to gene drive technologies, however, these phased testing programmes are likely incapable of providing the necessary risk reduction *and* the required data.

Phased testing programmes usually reduce risk by preventing the proposed organism persisting within the release environment. Avoiding persistence is achieved by a range of techniques, including the use of sterile insects for initial environmental releases.[82] However, in the

[75] Science and Technology Committee, *GM Insects* (HL 2015-16) 68-I, 30.
[76] British Ecological Society, 'British Ecological Society (BES) – Written evidence (GMI0024)' (British Ecological Society, 2016) 7.
[77] Rothamsted Research, 'Rothamsted Research – Written evidence (GMI0007)' (Rothamsted Research, 2016) 3.
[78] The Pirbright Institute, 'The Pirbright Institute – Written evidence (GMI0019)'(The Pirbright Institute, 2016) 2.
[79] Wellcome Trust, 'Wellcome Trust – Written evidence (GMI0025)' (Wellcome Trust, 2016) 3.
[80] ACRE, 'Advisory Committee on Releases to the Environment (ACRE) – Written evidence (GMI0014)' (ACRE, 2016) 3.
[81] NASEM (n25) Chapter 5; See also: Zach Adelman, Omar Akbari and Chris Wozinak, 'Rules of the Road for Insect Gene Drive Research and Testing' (2017) Nature Biotechnology 716.
[82] For instance, this has been the approach Target Malaria have taken in their initial field releases in Burkina Faso.

context of gene drive technologies, using sterile insects to gather data is self-defeating. It is the ability of the gene drive technologies to persist and self-sustain within the receiving environment and beyond which differentiates it from other transgenic insect technologies and render it useful as a population control technique. It is the ability of gene drive technologies to persist within the release environment that embodies both the technologies' benefits and its risks. Data concerning the persistence of gene drive organisms is precisely the data necessary for making informed decisions about gene drive technology. If a programme of phased testing is to provide reliable data useful for regulatory decision making, it cannot avoid the technology's persistence but must instead investigate the effects of persistence. Given that the possibilities for reducing risk during research, testing and development are constrained by the technology itself, there is a real need to reconceptualise the way we frame the way in which we develop our understanding of these technologies. Put differently, gene drive technologies by their nature challenge any attempts at a Rational-Instrumentalist paradigm understanding of science in regulatory decision making. The uncertainties surrounding gene drive technologies cannot be diminished by analytical methodologies alone, but instead require substantive deliberation on a range of values.

The debate about the relative merits of the European Union's current approach to risk and an approach that integrates risk and benefit has, elsewhere, been characterized as a battle between the precautionary principle and risk/benefit analysis.[83] Risk/benefit analyses involve complex issues around the appropriate role of the State in deciding what risks are acceptable in the pursuit of certain benefits – questions that present themselves as particularly profound in the context of gene drive technologies. Developing frameworks for understanding and delineating between tolerable and unacceptable risks inevitably requires normative judgments regarding the acceptability of harms to which citizens are exposed. However, the existing frames surrounding

[67] Cass Sunstein, 'Beyond the Precautionary Principle' (2003) *University of Pennsylvania Law Review* 1003.

'green biotechnologies' – the frame into which gene drive technologies are swept – obscure these difficult questions.

4.3 No Post-Release Regime of Liability

As discussed, albeit briefly, in the preceding chapter, there has been little thinking about liability for harms caused by the release of gene drive technologies. However, understanding whether harms might be compensated and if so, how, is an important part of the way that we frame and manage novel technologies. As Maria Lee points out, perceptions of the suitability of an authorization procedure will depend at least in part on our assessments of the post-authorization framework.[84] The post-authorization framework concerns itself with issues of risk management, efficacy monitoring, maintenance, cost and liability. As such, decisions to authorize risky activities, depend, in part, on how we foresee those risks being managed, and how we might make good the harm that occurs if and when those risks materialize. Furthermore, the presence or absence of a framework for rectifying harms caused by gene drive technologies, particularly during the research phase, has implications for the ethical quality of research conduct – this is a theme that we will refer back to in Chapter Seven.

4.3.1. Liability for What?

As was outlined in greater detail in Chapter Two, the potential harms that might be caused by gene drive technologies vary. One example might be individuals contracting more aggressive forms of the disease that a gene drive has been built to prevent. In the context of malaria, we know that the *Plasmodium* parasite is a rapidly evolving organism, capable of developing resistance over short periods of time.[85] This knowledge has led to speculation regarding two possible consequences of gene drive resistance:[86] first, the causing of a boom in the mosquito population leading to an increased disease burden and thus a higher frequency of malaria within the human population;

[84] Lee (n72) 104.
[85] Robert L. Unckless, Andrew G. Clark and Philipp W. Messer, 'Evolution of Resistance Against CRISPR/Cas9 Gene Drive' (2017) *Genetics* 827.
[86] The development of gene drive resistance is a highly complicated area of molecular biology, however some overview will be given in the thesis.

second, and more relevant to the issue of liability, the causing of more aggressive strains of malaria that, once contracted, cause more harm to the sufferer. This increased harm may present by way of longer recovery times, increased rates of neurologic defects and vital organ dysfunction.[87] In case of this eventuality, this would, in turn, cause higher rates of mortality in pregnant women, children and migrants originating from non-endemic regions.[88] In these cases, we might expect individuals to claim for physical harm, pain and suffering and any consequential economic loss. Gene drives built to combat pests and pesticide resistance may cause environmental or ecological harms such as crop failure. For example, crops might fail as a result of gene drive resistance and thus cause an increase in the pest population. This may occur where a gene drive is designed to confer extreme susceptibility to insecticides on a pest population. Whilst the gene drive works, the numbers of crop pest are reduced and crop yield increases. If the target organism develops resistance to the drive, the pest is no longer susceptible to the insecticide, the pest population increases and, without the protection of insecticides, the crop succumbs to pest damage. In terms of practical consequences, in the non-gene drive context the analogous scenario would be one in which a company supplies a faulty batch of insecticides, leaving the sprayed crop without protection from pests. For gene drive technologies, such a scenario will likely affect all agricultural activity in a given area, thus failing to discriminate between farmers who consent to, or oppose, the gene drive release. Those cultivating crops who suffer crop failure as a result of gene drive might be expected to make a claim for property damage and consequential economic loss.

Despite the very real threat of these harms, the current GMO framework provides no regime of liability if gene drive technologies cause harm post-release.

[87] World Health Organisation, *Guidance for the Treatment of Malaria* (World Health Organisation, Third edn 2015) 24-25. http://apps.who.int/iris/bitstream/10665/162441/1/9789241549127_eng.pdf?ua=1&ua=1
Last Accessed 10th May 2017.
[88] ibid 48.

4.4 Genetically Modified Organism Definition Objection

Not all GM insects are gene drives and not all gene drives use GM insects. This is often a point of confusion amongst regulators, lawyers and social scientists. Conflation of the two has been surprisingly frequent in the literature as well as academic discussions of gene drive technologies.

For example, in their piece in the *American Journal of Bioethics*, R. Atla Charo and Hank Greely discuss the use of CRISPR gene editing technologies for novel forms of disease prevention.[89] Throughout the discussion of the applications of CRISPR technologies and the associated regulatory gaps, Charo and Greely focus on Oxitec's OX513A mosquito (a non-gene drive, non-CRISPR insect), failing to distinguish between that organism and gene drive systems (CRISPR-based or otherwise).[90]

Whilst it might be true that a regulatory framework suitable for gene drive would also manage the risks of GM insects such as Oxitec's OX513A, the inverse is not true. The nature and extent of the risks associated with gene drives as compared to GM insects are far greater and often more uncertain. Unlike gene drive systems, GM insect releases are self-limiting and reversible. Regulating the two technologies under the same framework would be an instance of regulatory overkill, stifling innovation and progress in the field of GM insect research. Equally, to regulate gene drive as a GM insect technology not only falls foul of the definitional difficulties outlined below, but also fails to recognise and manage the risks and ethical implications unique to this technology. Thus, when considering regulation in this context, clarity and precision are vital in defining the target of legal regulation.

Further, as was suggested in Chapter Two, not all gene drive systems consist of genetically modified organisms under the statutory definition. Article 2(b) of the Contained Use Directive prescribes a list of techniques, detailed in Annex 1A, Part 1, that result in the production of genetically modified organisms. Whilst many of the techniques used to build gene drives fall within

[89] R A Charo and H Greely, 'CRISPR Critters and CRISPR Cracks' (2015) *American Journal of Bioethics* 11, 13.
[90] ibid 13-15.

the scope of the Act, at least one gene drive system, the *Wolbachia* Drive, sits entirely outside the regulatory framework.[91]

Wolbachia Drives are built by inserting *Wolbachia* bacteria into the host organism - in this instance *Aedes aegypti* mosquitos.[92] *Wolbachia* is a type of commonly occurring bacteria known to infect a high proportion of wild insect populations. The *Wolbachia* bacteria interfere with the host organism's reproductive biology preventing the birth of live young and thus creating a population suppression drive. Paradoxically, because the technique entails the introduction of a whole genome (the *Wolbachia* genome) rather than the insertion of single genes, it does not fall within the scope of the legislative definition of genetic modification laid out in Article 2(b) of the Contained Use Directive.[93]

Despite this regulatory inconsistency, gene drives built using non-GM techniques (like the *Wolbachia* system) carry the same risks and safety concerns as their GM counterparts. For example, research has demonstrated that much like genetically engineered drive systems, *Wolbachia* drives have the potential to be highly invasive, self-sustaining and irreversible.[94]

4.5 The Status of Field Trials: Contained Use, or Deliberate Release?

As GM insect research has gained pace, new research pathways and protocols have emerged in response to the risks presented by a highly mobile and fast reproducing class of organism. Where previously in plant-based research contained laboratory use followed by small open field trials was sufficient to observe and manage the risks posed by the accidental or deliberate release of the proposed organism, the same is not true of GM insects, and by extension, gene drive research.

The scientific community has begun to utilise what they term 'caged field trials' or 'semi-field conditions' in their step-wise assessments of GM insects.[95] However, legal the status of 'caged

[91] For a more scientific discussion of the bio-molecular differences between gene drive systems and the implications for regulation, see: Shraddha Chakradhar, 'Buzzkill: Regulatory Uncertainty Plagues Rollout of Genetically Modified Mosquitos' (2015) 21 Nature Medicine 416.
[92] L Alphey et al, 'Genetic Control of *Aedes* mosquitoes' (2013) *Pathogens and Global Health* 170, 174-176.
[93] Council Directive 2009/41/EC, (n33) Art 2(b).
[94] L Alphey, 'Genetic Control of Mosquitoes' (2014) Annual Review of Entomology 205.
[95] Lucas Facchinelli et al, 'Field Cage Trials and the Progressive Evaluation of Genetically Modified Mosquitos' (2013).

field trials' as instances of either contained use or deliberate release has significant consequences for risk management. These caged field trials, recommended in the World Health Organisation's 'Guidance Framework for Testing of Genetically Modified Mosquitos', provide a more realistic assessment of the characteristics of GM insects in the wild than can be gained in the laboratory.[96] Given that the data these trials provide play an important role in understanding and managing the risks associated with gene drive, these caged trials *should* form a part of any step-by-step approach to responsible gene drive research.

However, in providing more realistic and useful data, caged field trials pose higher levels of risk than those observed under the contained laboratory conditions provided for by Contained Use Directive 2009/18/EC. Caged field trials use far larger numbers of insects whilst using containment measures more susceptible to breach. Field cages are more prone to structural failure due to the increased exposure to environmental damage (for example wind, rain or lightning) or damage caused by wild animals. Furthermore, field cages are more difficult to protect from deliberate acts of sabotage or vandalism – two problems far from alien in the GMO context.[97] Finally, there is a risk of the contained GM insects mating with their wildtype counterparts through the mesh walls of the cages, thus allowing a gene drive to propagate without the actual escape of research organisms.

From a regulatory perspective, the difficulty arises when we consider the status of caged trials with reference to the Contained Use and Deliberate Release Directives. The Directives, having been devised with different levels and types of risk in mind, subject notifications to varying levels of scrutiny. As such, whether caged field trials fall to be considered as instances of contained used or deliberate release has practical implications for the assessment and management of risk, and the protection of human, animal and environmental health. As instances of research activity

PLoS Negl Trop Dis 7(1) e2001; Ng'habi et al, 'Colonization of malaria vectors under semi-field conditions as a strategy for maintaining genetic and phenotypic similarity with wild populations' (2015) *Malaria Journal* 14:10.

[96] WHO/TDR, 'Guidance Framework for Testing of Genetically Modified Mosquitos' (2014).

[97] For an instance of deliberate interference with GMO research, resulting in charges for criminal damage see: *R v Bellotti, Melchett and Others* (2000) Norwich Crown Court.

carried out under specific controls (i.e. mesh cage structures) adopted for the purpose of limiting contact between the organism and the environment, caged field trials fall within the legislative definition of contained use.[98]

As a consequence, contained field trials are subject to less stringent risk assessments and lower informational requirements, despite bearing levels of risk more akin to those envisaged by the Deliberate Release Directive.[99] For the reasons drawn out above, caged field trials are far more susceptible to incidences of accidental release than the more stringently controlled traditional contained use phase of research. Given that mathematical models predict that the escape or release of as few as five gene drive mosquitos might result in the alteration or suppression of *entire* populations, it is not clear that for gene drive technologies caged field trials can be considered materially less risky than instances of deliberate release.[100] Perhaps the starkest illustration of the inadequate regulatory oversight for contained field trials is the absence of a specific environmental risk assessment such as that required for deliberate release, under Article 6(2) of Directive 2001/18/EC. Thus, if caged trials are considered instances of contained use – as well they might be given their fidelity to the legislative definition – these risky activities will take place in the absence of environmental risk assessment.

Furthermore, this problem is not one unique to regulation in European Union Member States. Burkina Faso and Mali, the countries currently predicted to be the first States to release a gene drive, employ similar definitional categories. In Burkina Faso, Law No 064-2012/AN,[101] sets out a framework for contained use and deliberate release, mirroring the European Union System.

[98] The Definition of Contained Use can be found in Article 2(c) of the Contained Use Directive, closely modelled on the definition adopted in Article 3(b) of the Cartagena Protocol.
[99] For an illustration of the different risk assessment and information requirements compare Annex III, sections A and B, Council Directive 2009/18/EC and Annex II, section D, Council Directive 2001/41/EC.
[100] John M Marshall and Omar S Akbari, 'Can CRISPR-based gene drive be confined in the Wild? A Question for Molecular and Population Biology' (2018) ACS Chemical Biology 424.
[101] Law n° 064-2012/an, - *establishing a regime of safety regulations in the area of biotechnology*. [Burkina Faso]

In Mali, Law n°08-042/AN,[102] Article 2(x), also provides for a framework divided between contained use and deliberate release.

Given that the current legal categories of contained use and deliberate release have practical implications for the assessment and management of risk, real consideration must be given to the suitability of this bi-partite system of regulation. Gene drive technologies, by their ability to spread and persist in the wild, destabilize the assumptions underpinning the Contained Use and Deliberate Release directives. The failure to recognise these distinct and challenging features of gene drive technologies is very much a failure of framing – a failure to identify and accommodate a range of novel overflows.

However, resolving the matter is unlikely to be as simple as requiring the assessments currently performed for deliberate release to be performed at the earlier contained use stage. Such a requirement would have severe economic effects on the small research institutions carrying out this research. Thus, the possibility of a regulatory solution capable of adequately assessing and managing risk without stifling innovation must be explored.

5. Returning to Regulatory Connection & Framing

The analysis in the last section focused on four discrete ways in which the overly narrow frame constructed around the regulation of GMOs presents challenges for the regulation of gene drive technologies. However, the mere existence of challenges that result from overly narrow frames does not automatically necessitate regulatory overhaul. Some of the challenges posed by emerging technologies might be dissolved by means of reasoned judicial innovation rather than wholesale reframing and the associated legislative intervention. How then, might we sort those challenges that require a ground-up reconsideration of the frames that we adopt from those that might be resolved by the Courts?

[102] Loi n°08-042/an, – *rm du 1er decembre 2008 relative à la sécurité en biotechnologie en république du mali. l'assemblee nationale.* [Mali]

This section argues that Roger Brownsword's taxonomy of 'regulatory connection' presents a useful means of interrogating how well our existing frames are built, and whether, in the face of technological innovation, they are fit for purpose. Brownsword demonstrates that in understanding the role and response of law in addressing regulatory challenges and thus achieving 'regulatory connection', we first have to understand the nature of the disconnection.[103] Firstly, we must ask whether an instance of disconnection is 'descriptive' or 'normative',[104] that is, whether the problem is one of covering descriptions utilised by the regulatory framework no longer corresponding to the technology, or whether it is the value judgements underlying the regulatory scheme that are no longer adequate.[105]

Once that question has been answered, we must ask whether the challenge under examination is an instance of 'productive' or 'unproductive' disconnection.[106] Where there is a genuine uncertainty as to whether the new technology falls within the spirit and intent of the regulatory framework, the disconnection is said to be productive. On the other hand, when the use of legal and regulatory resource in translating unproblematic regulatory intent into regulatory letter is wasteful, the disconnection is said to be unproductive.

Classifying incidents of disconnection in this way has consequences for how we approach the issue of reconnection. As Brownsword demonstrates, the classifications that we assign determine whether reconnection can be achieved by means of intelligent 'purposivism' or whether the issue is, instead, one ripe for more general legal debate or reframing.[107] In the context of discussions about well-built frames, I argue that those frames that result in normative disconnections are those that require reconsideration.

Gene drive presents a whole host of 'disconnections', four of which were noted in Section Four above. However, as was suggested earlier, the nature and function of these disconnections

[103] Roger Brownsword, *Rights, Regulation and the Technological Revolution* (Oxford University Press 2009) 160-184.
[104] ibid 166
[105] ibid.
[106] ibid 166-167.
[107] ibid 167.

vary, bearing quite different implications for the regulatory frames that they challenge. For example, the fact that the legislative definition of genetic modification fails to encompass *Wolbachia* drives is an instance of disconnection quite different from the one presented by the statutory approach to risk. Applying the lens of Regulatory Connection, the former case is one of a mismatch between covering descriptions; questions surrounding the definition of 'genetic modification' possess no moral dimension. The mismatch is descriptive and unproductive. Thus, bringing *Wolbachia* drives under the auspices of the Contained Use and Deliberate Use Directives might be achieved by an exercise in purposive interpretation.[108]

If purposive interpretation was the solution in all the instances of disconnection discussed so far, one might think that the legal regulation of gene drive was simply a matter for the Courts to resolve through steady, careful and intelligent judicial innovation, rather than consideration in academic legal scholarship. However, the risk-based objection discussed above poses quite a different form of disconnection. Gene drive technologies present risks far greater than those associated with GM crops, the organism around which the legislation was drawn up.[109] Conversely, they also provide public health benefits inconceivable at the time the legislation was drafted. Thus, the disconnection here is not merely descriptive, but normative – it destabilizes settled assumptions about what harms might be tolerated in the pursuit of a legitimate public health benefit. This disconnection raises questions, new and old, about what measures a State might impose on its citizens. For these reasons, the disconnection described is normative. Moreover, these questions do not fit within the spirit and intent of the regulation. They are issues that cannot be resolved by merely adopting a purposive interpretive approach, but instead warrant further debate. In this way, the need for reframing – a reconsideration of the overflows, target agents and source agents that a system of regulation ought to take account of – becomes apparent. In order

[108] Council Use Directive 2009/41/EC (n33); Council Directive 2001/18/E (n33).
[109] Lee (n1).

to achieve the regulatory connection that we are striving for, we need to build frames that take account of the normative features of the picture that current regulation leaves out.

As such, when thinking about the regulation of gene drive technologies – or the regulation of emerging technologies more generally – we might recognise Brownsword's taxonomy of Regulatory Connection and the methodology of framing as complementary. Understanding the importance of well-constructed frames does little to help us identify which frames, once built, are robust enough to incorporate the relevant range of overflows, target agents and source agents. However, where normative disconnections arise, we can be satisfied that the dominant frame is too narrow to reflect and manage the full range of concerns that the new technology confronts us with. Similarly, the methodology of framing provides a way forward once normative disconnections have been identified. Regulators, scientists, lawyers and policy makers alike ought to understand normative disconnections as a call for reframing, a fresh consideration of all of the overflows that the technology presents. As such, the methodology of framing goes some way to fleshing out what ought to be done once normative disconnections have been identified. Chapters Six and Seven further develop an account of what reframing requires.

This Chapter has applied the methodology of framing, and Roger Brownsword's taxonomy of Regulatory Connection, in order to demonstrate that the regulation currently tasked with regulating gene drive technologies – in the European Union at least – is radically unfit for that purpose. This is, in no small part, due to the fact that the technical assumptions about the similarities between GMOs and gene drive technologies dwarf non-technical considerations that reveal another, distinct understanding of gene drives as a regulatory object. Whilst this Chapter has described an instance wherein the legal culture has failed to build a frame that bears fidelity to the realities of the regulatory object (in this case gene drive technologies), the Chapters that follow think about the ways in which lawyers can, and have, built better frames.

CHAPTER FIVE: LEARNING LESSONS FROM PUBLIC HEALTH LAW

Chapter Three described the folly of narrow frames and lawyers' failures to take responsibility for overseeing the ways in which knowledge about certain challenges (in this case gene drive technologies) is gathered, structured and deployed. Chapter Four concerned itself with an analysis of the particular problems that result from narrow frames in the regulation of gene drive technologies. This Chapter sows the seeds for a way forward, which promises to build a frame for understanding gene drive technologies bearing fidelity to the various complexities that they present. In that way, this Chapter functions as a bridge, connecting the problematic contemporary framing of gene drive technologies to the means by which we might frame them better. Much of this bridging exercise consists of considering the valuable lessons that might be learnt from other areas of law and regulation.

This Chapter demonstrates that although lawyers might find calls to engage in framing or to take collective epistemic responsibility confronting, in some sectors lawyers are doing this sort of work already. As such, this Chapter engages in a discussion of public health law and reflects on the way that lawyers working within this field can be seen to have developed robust frames for a range of deeply challenging and complex legal and social problems. These frames are not dogged by demands for narrow technical expertise but are instead informed by a great range of values, considerations and knowledge claims. Put differently, the theoretical understanding of public health law developed within the academic scholarship and the actualities of its practice identifies and manages a broad range of overflows and multiple populations of target agents, oftentimes with varying interests. In many of the examples discussed below, public health laws step beyond understandings of the world and decision-making dictated by technical expertise and quantifiable measures of harm, derived from technical analytical methodologies. Public health law has, for the most part, eschewed the Rational-Instrumental model of decision making and instead oftentimes relies on the assimilation of a range of diverse knowledge claims, hailing from all manner of

expertise. Unlike the regulation of biotechnologies, public health law has avoided siloing the issues with which it is confronted into pre-existing frames, red or green or otherwise, and has, as such, avoided any overzealous gatekeeping of the knowledge claims and expertise that might be taken account of in decision making.

In places throughout this Chapter, I note the ways in which particular commitments of public health law might be helpful to our thinking about the proper regulation of gene drive technologies. However, my intention here is not to suggest that public health law offers up a complete roadmap to the safe and effective regulation of gene drive technologies. Instead, the primary aim of this Chapter is to consider the lessons that we might learn from our colleagues in public health law, when it comes to building robust frames in areas of high technological complexity. These lessons assuage concerns that pleas for lawyers to engage in framing, or pleas for them to take collective epistemic responsibility, are generated by close minded idealism or naivety as to the lawyer's task. Rather, examples of lawyers doing just those things exist out there in the real world of policy making, statute writing and law enforcement.

What follows proceeds thusly. First, I explore the normative conception of public health law laid out in the work of Lawrence Gostin and track the ways in which it provides an example of how robust frames come to be developed by lawyers. In particular, I demonstrate the ways in which the normative commitments of public health law play a role in identifying overflows, target agents and source agents that technical understandings of gene drive technologies fail to flag. The core commitments laid out by Gostin motivate understandings of technological phenomena that extend beyond their 'technical sweetness'[1] but instead are constructed by asking questions about their social, political, cultural and legal implications.

Moving on from the theoretical discussion of public health law, the next section provides an analysis of the ways in which public health law has built broader frames in practice. I offer two

[1] Kevin Esvelt, 'Gene Editing Can Drive Science to Openness' (*Nature World View*, 9 June 2016) https://www.nature.com/news/polopoly_fs/1.20043!/menu/main/topColumns/topLeftColumn/pdf/534153a.pdf Last accessed 5th September 2019

cases studies (the legislation enacted during the sanitary movement and water fluoridation legislation) in order to demonstrate how public health law can illuminate understandings of the way lawyers engage in framing. These two legislative frameworks demonstrate the ways in which the social, cultural, political and legal implications of certain technological propositions (sewers and water fluoridation) have been built into the frames used to describe them as regulatory objects. In this connection, I suggest that public health law and its commitments provide at least a useful starting point for thinking about the regulation of gene drive technologies. To be clear, I am not offering public health law up as some utopia in which the construction of imperfect frames is impossible and all descriptions of regulatory object are mirror-like in their fidelity to representation. Instead, I suggest that the study of public health law is a good way to learn lessons about how lawyers can and have built better frames.

1. Introduction to Public Health Law and Ethics

Public health law has some history of creating robust frames that admit of the complexity of the phenomena that they regulate. Lawrence Gostin's seminal work on public health law defines the discipline as follows:

> Public health law is the study of the legal powers and duties of the State in collaboration with its partners (e.g., health care, business, the community, the media, and academia), to ensure the conditions for people to be healthy (to identify, prevent, and ameliorate risk to health in the population), and of the limitations on the powers of the state to constrain for the common good the autonomy, privacy, liberty, proprietary, and other legally protected interests of individuals. The prime objective of public health law is to pursue the highest possible of physical and mental health in the population, consistent with the values of social justice.[2]

For Gostin, then, public health law is concerned with the seven following core themes or commitments; first, the obligations of States in respect of health; second, the limits on State powers in respect of health; third, the identity, responsibilities and powers of those non-governmental partners capable of affecting population health; fourth, a focus on populations rather than persons;

[2] Lawrence O. Gostin, *Public Health Law: Power, Duty, Restraint* (Berkeley: University of California Press 2nd edition 2008) 3. Interestingly, in the third edition of the same text, Gostin, along with his co-author, Lindsay Wiley, removes mention of both the importance of governmental partners and community participation from the definition of public health law. See: Lawrence O Gostin and Lindsay F Wiley*, Public Health Law: Power, Duty and Restraint* (Berkeley: University of California Press 3rd edition 2016) 4. The *Preface* to the third edition does not speak to this editorial decision.

fifth, the importance of community participation in public health interventions; sixth, a focus on prevention rather than cure; and seventh, a commitment to social justice. Worth noting at this point is the way in which many of the commitments that Gostin's work takes up cannot be subjected to quantification or measurement. In this way, public health law eschews the dominance of technical expertise and the rational-instrumental approach to decision-making, instead embedding the framing process with questions of value. On Gostin's account, public health law is not constrained to thinking about measures of health, safety and risk alone, but instead considers them and how they interact with the social, political and cultural structures they arise within. Later in this Chapter, and continuing on in Chapters Six and Seven, I move on to chart the way in which questions of value and substantive ethical enquiry can place on screen a range of otherwise overlooked overflows, target agents and source agents.

Gostin's work on public health law in particular is of an American persuasion but the core concerns that his definition reflect are common to most anglophone understandings of public health law. This is brought out by John Coggon when he surveys the definitions of public health law proffered by UK textbooks on medical law.[3] Notably, common to all of the definitions he reviews are: an understanding of public health law as a constraint on state powers (particularly true for Jonathan Herring, who conceives of inquiry into legitimate governmental policy as a central commitment);[4] concern for the state-citizen relationship (a function of the previous concern, but also reflecting an understanding of the state as holding positive obligations with regard to citizen's health); an understanding of the varied sources of public health law (public health law exists beyond statute, found also in governmental policy, professional guidelines and regulation); and, finally a reflection on the tension between the interests of individuals and the interests of the population and the attainment of the common good.

[3] John Coggon, What Makes Health Public? A Critical Evaluation of Moral, Legal and Political Claims in Public Health (Cambridge University Press 2012) 88-91.
[4] Jonathan Herring, *Medical Law and Ethics* (Oxford: Oxford University Press, 7th edn 2018) 17.

2. Public Health Law and Broader Frames

This section considers the ways in which the core commitments animating public health law, as described within the scholarship, implicate some of the most challenging aspects of gene drive technologies. Drawing these animating commitments from Gostin's work, this section discusses the way in which public health law requires and scrutinises a variety of expertise and values in decision-making and thus is capable of building broader frames for understanding the complexity of the phenomena with which it is faced. In this way, public health law is able to identify overflows, source agents and target agents that go overlooked when regulatory decision making is predicated on technical expertise alone. What follows looks at the identification of three elements that have recurred throughout the analysis so far – overflows, target agents and source agents – and considers how the approach of public health law broadens the analysis undertaken.

2.1 Public Health Law & Overflows

This section discusses the way in which two of public health law's core commitments as described by Gostin – community participation and a preference for prevention – require us to ask a broad range of questions about the uses and implications of gene drive technologies. I highlight the ways in which these questions identify a range of overflows that would not otherwise be observed and are not accessible through scientific findings and technical expertise alone.

2.1.1 Community Participation & the Identification and Avoidance of Overflows

Public health law's concern to support and facilitate community participation in the development and deployment of public health initiatives influences the way in which we frame those novel technologies. By engaging with communities, those concerned with developing sound regulatory responses have the opportunity to identify overflows that might otherwise go overlooked.

Recall Chapter Three's discussion of the range of overflows that have been overlooked in various other contexts. One example was the communities on the shores of Lake Victoria using their mosquito bed nets as fishing nets. This caused two unanticipated overflows: firstly, fish stocks were vastly reduced due to the fine mesh of the nets catching juveniles that would not be caught

in conventional nets; secondly, as the bed nets were not being used for their intended purpose, disease burden was not being reduced.

Careful community engagement can identify these otherwise overlooked overflows and thus play a significant role in bridging the epistemic gaps challenging the regulation of gene drive technologies. Community engagement procedures that recognise target agents as more than potential malaria sufferers or beneficiaries of the proposed technology can put novel overflows on screen. Engaging with communities and their own accounts of their most pressing needs provides the opportunity to make otherwise 'unpredictable' human behaviours foreseeable. In this way then, good community participation procedures identify overflows that would otherwise be left out of the frame we construct in order to understand the implications of new technologies – implications that exist far beyond the reach of technical expertise alone.

Secondly, not only does community engagement identify overflows that otherwise go overlooked but also helps to avoid one overflow in particular – regulatory failure. In the first instance, and with regard to the regulation of public health interventions, effective community participation builds public perceptions of the moral legitimacy of public health interventions and the process of their implementation. Secondly, and relatedly, community participation has been shown to increase the efficacy of public health interventions. This increased efficacy is explainable in two ways. First, those measures which have been developed and introduced through a system of community participation are perceived by the population to benefit from a higher degree of legitimacy. Perceptions of legitimacy are themselves good barometers for efficiency. As Brownsword and Goodwin note:

> Perceptions of the moral legitimacy of the regulatory instruments and regimes go therefore not only to the efficiency of the instruments themselves but to matters of social and political cohesion and ultimately to the (self-) identity of the community itself.[5]

[5] Roger Brownsword and Morag Goodwin, *Law and the Technologies of the Twenty-First Century* (Cambridge University Press 2012) 172.

Thus, public perceptions of legitimacy can and do have real implications for the efficiency of regulation and the efficacy of the intervention that the regulation prescribes. The relationship between public perceptions of legitimacy and regulatory efficiency has been demonstrated in practice – the most obvious example being the breakdown of the European Union's regulation of Genetically Modified Organisms.[6] Ultimately, in the face of scant public support and rife public criticism the European Union entered into a *de facto* moratorium on the licensing of new GMOs.[7] The lack of a mechanism for community participation in regulatory decision-making has regularly been cited as instrumental in the failure of the European Union's first suite of GMO legislation.[8]

Beyond legitimacy as a determinant of a public health intervention's efficacy, however, research demonstrates that communities that are engaged and consulted during the development of public health interventions are more invested and, in turn, more compliant with the prescribed measures. Higher rates of engagement and compliance consequently fuel the efficacy of the intervention. As Gostin points out, this effect has been most obviously noted in the context of public health authorities adopting 'a kind of deliberative democracy' in their approach to introducing public health interventions.[9] As such, community engagement can avoid regulatory failure causing a broad range of further overflows.

Finally, community participation and consultation require us to think explicitly about the ways in which we build our frames of understanding. In part, and, as F. Douglas Scutchfield, Carol Ireson and Laura Hall point out, this is because before community participation and public deliberation can take place, we are forced to frame the issue in the 'meaningful context of everyday life'.[10] In order to engage with communities about the technologies we propose to use, we must

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[6] On this issue, see: See, for example: Grace Skogstad, 'Legitimacy and/or Policy Effectiveness?: Network Governance and GMO Regulation in the European Union' (2001) Journal of European Public Policy 321.
[7] Regarding the nature of the moratorium see: Sarah Lieberman and Tim Gray, 'The So-called "Moratorium" on the Licensing of New Genetically Modified (GM) Products by the European Union 1998–2004: A Study in Ambiguity' (2006) 15 *Environmental Politics* 592.
[8] Maria Lee, EU Regulation of GMO's: Law and Decision Making for New Technologies (Cheltenham, Elgar Publishing 2008) 243.
[9] Gostin (n2) 18.
[10] F Douglas Scutchfield, Carol Ireson and Laura Hall, 'The Voice of the Public in Public Health Policy and Planning' (2005) Journal of Public Health Policy 197, 198.

provide them which descriptions of the technology, in order that they might make decisions about it. Rendering these descriptions whilst also taking account of the meaningful context of everyday life is itself crucial to the framing process. This pre-deliberative framing exercise itself requires us to identify the advantages and disadvantages of the technology, the trade-offs we have to make and the weight of the moral and ethical considerations we are faced with. That is, the very process of engaging communities requires us to reflect, explicitly and self-consciously, about the ways in which we frame the technology.

Whilst the information gathered by the community engagement process likely changes the contours of the frame that we ultimately adopt (by identifying new overflows, or target agents) it does re-enforce the need to reason carefully and explicitly about the ways in which we build frames. Importantly, the determinations of relevant overflows rendered by the community participation process are not of the abstract sort that we have hitherto dealt with in this thesis. Rather, they take into account the precise situation of the target community. As such, effective community participation procedures require advanced ethical thinking and real commitment to the framing exercise.

2.1.2 Preference for Prevention & Identification and Avoidance of Overflows

Very often, when distinguishing between the practice of medicine and public health, commentators point to the difference between amelioration and prevention.[11] Whilst doctors practicing medicine are in the business of treating and curing the already sick, public health aims to prevent sickness in the first place. Thinking about just a few public health initiatives, the prevention orientation is clear: water fluoridation for the prevention of dental caries; vaccination for the prevention of communicable disease and sugar taxes for the prevention of obesity.

[11] Gostin (n2); Geoffrey Rose, 'Sick Individuals and Sick Populations' (1985) International Journal of Epidemiology 32, 37; Coggon (n3).

Nevertheless, some argue that this alleged bright line between prevention and amelioration is not as bright as the advocates of a prevention orientation suggest.[12] To be sure, some public health laws and policies do aim toward cure rather than prevention. This is especially true when we think about policies concerned with the funding of health care provision. Any public health policy seeking to ensure access to healthcare to individuals who would otherwise be unable to afford it, *is* predominantly ameliorative. For our purposes we need not linger too long on the clarity and ubiquity of this distinction in public health more generally. In the context of gene drive technologies, we can straightforwardly understand their use as preventive, in the same way that we would understand the use of pesticides to be preventative. The preventive dimension then, possesses certain features salient to the discussion of framing.

In the first instance, and as Gostin points out, preventive measures are almost exclusively more cost-effective than ameliorative ones.[13] Gene drive technologies as a response to vector-borne disease are no different in this respect. Like other preventative public health measures, gene drive technologies promise a favourable cost-benefit ratio. The eradication of malaria will always be more cost effective than actively treating its symptoms once people become sick, and that is without taking into account the wider effects that sickness has on the economy, due, for example, to inability to work. In this sense, on an economic analysis, gene drive technologies will likely always present the most desirable solution to vector-borne disease. Twenty years ago, the direct costs of malaria paid by African states was estimated to be over $12 billion annually.[14] With regard to individual States, figures vary depending on the extent of disease burden. In Ghana, malaria associated costs made up 0.41% of Gross National Product (GDP), whereas in Chad the figure is

[12] Louise B Russell, 'Prevention v. Cure: An Economists Perspective' in (eds) Halley S Faust and Paul T Menzel, *Prevention vs. Treatment: What's the Right Balance?* (Oxford: Oxford University Press 2011).
[13] Gostin (n112) 21.
[14] J Sachs and P Malaney, 'The Economic and Social Burden of Malaria' (2002) Nature 680.

close to 9% of GDP.[15] Further, those countries with a high disease burden are found to suffer a GDP up to five times lower than that of their non-malarial counterparts.[16]

As such, gene drive technology's prevention orientation presents not only the opportunity for vast improvements in population health, but also the chance for hitherto unrealised economic growth and development. For these reasons, governments have rational, perhaps even irresistible, economic reasons for deploying gene drive technologies. Thus, in the first instance, public health's preference for prevention must also challenge public health law to avoid what might be myopic, economically driven decision-making. Whilst there is and should be room for economic analysis in decision making around the regulation of new technologies, these economic ideals should not be sovereign, and it is for public health law to balance economic interests against the other interests discussed in this Chapter. In this way, then, the preference for prevention puts the economic aspects of the technology, as overflows in and of themselves, within the frame, but in such a way as the economic benefits are also held up against the range of other values and possible world states.

Secondly, public health's preference for prevention provides another implication from the perspective of framing. The preference for prevention requires an inherently forward-looking approach to the identification and evaluations of overflows and potential overflows, but it also requires that we compare the desirability of existing world states and those that the technology in question might bring about.

2.2 Public Health Law & Target Agents

This section discusses the way in which public health law's focus on populations rather than individual persons requires us to ask a broad range of questions about the uses and implications of gene drive technologies. I highlight how understanding the population focus of public health

[15] African Union, "Gene Drives' for Malaria Control and Elimination in Africa' (2017) 6.
[16] W Jobin, 'Suppression of malaria transmission and increase in economic productivity in African countries from 2007 to 2011' (2014) Malaria World Journal 1.

and gene drive technologies can illuminate our understanding of the complex range of target agents that might be affected by the deployment of these technologies.

2.2.1 Populations Rather Than Persons, and Target Agents

The focus on populations rather than individual persons is what fundamentally distinguishes public health practice from the practice of medicine. Similarly, what distinguishes medical law from public health law is that whilst the latter focuses on the relationship between the citizen and the State, the former focuses exclusively on the relationship between patient and doctor. Whilst doctors seek to understand the causes and cures for a particular patient's malady, public health is interested in the initiatives capable of improving the health of whole populations. Epidemiologist Geoffrey Rose describes public health's population focus as 'the attempt to control the determinants of incidence, to lower the mean level of risk factors, to shift the whole distribution of exposure in a favourable direction'.[17]

As such, and as Rose famously noted, given the statistical realities of health-affecting risk factors, public health initiatives necessarily intrude into the lives of persons at a low risk of disease or ill-health. In this way, public health laws prioritize populations over and above the interests or objections of individuals.

Public health laws have, in their promulgation, grappled with the tension between individual autonomy and the common good, ultimately resolving the conflict in favour of the common good and population health. Tensions between individual freedoms and the attainment of the foundational value of 'health' for populations are present in almost all public health debates, ranging from sugar taxes to water fluoridation, vaccination programmes to folate enrichment programmes.

The conflicts between populations and persons are particularly acute in the context of gene drive technologies in the following ways. In the first instance, current iterations of the technology

[17] Rose (n11) 37.

cannot be spatially limited or confined. Gene drive organisms, especially those difficult to contain (such as mosquitos and other small invertebrates), do not respect political boundaries. As such, whilst the persons in the geographical area in which gene drive organisms are originally released might benefit from their use, neighbouring communities not facing the same degree of disease burden might only experience ill-effects associated with the technology.

Furthermore, as was highlighted in Chapter Three, individual members of the same populations will benefit to differing extents depending on factors such as their age or pre-existing immunity. Therefore, given the technology's ability to spread, we are faced with the conflicts both within and *between* populations.

Secondly, given the scientific uncertainty surrounding both the efficacy of gene drive techniques in reducing disease burden *and* the risks that the use of the technology might pose, questions surrounding either the benefit of the intervention or the extent of the interference it introduces are hard to answer. The tensions that gene drive technologies engender between population health and individual interests are, for the most part, questions concerned with the just distribution of benefits and burdens. They are questions of social and distributive justice. Given that a further core concern of public health law is its social justice foundation, it already has at its disposal some tools for disentangling and beginning to answer these difficult questions. We will return to a more thorough examination of these issues in Chapter Seven.

Public health law's conscious focus on the interests of populations rather than persons puts on screen the complexity associated with identifying relevant target agents for the purposes of regulation. This sort of analysis is therefore able to recognise that different individuals and populations might be affected by different overflows and so brings into the frame a broad range of interests held by different persons and thus the range of target agents that might exist, and the differing levels of protection that they might require of regulation.

2.3 Public Health Law and Source Agents

This section discusses the way in which public health law's explicit focus on all health affecting actors and the limits of state powers poses a broad range of questions about the uses and implications of gene drive technologies. I highlight the ways these questions can illuminate our understanding of the vast range of source agents that might be implicated by or considered responsible for the safe and fair deployment of these technologies.

2.3.1 Partners in Public Health Law & Source Agents

Public health law has, for some time, understood the importance of assigning responsibilities for health to a multiplicity of actors within a public health system. In this way, then, public health law is well practiced in recognising a broad range of target and source agents as relevant to the frames of understanding that we adopt and the regulatory solutions that we pursue. As Gostin puts it:

> Governance for health is complex and multifaceted. A broad range of stakeholders exert considerable power over events that influence health. These stakeholders may act alone, in partnership, or in conflict; separately and together they influence the conditions in which people can be healthy or be placed at risk.[18]

Thus, governments and public health law must identify those actors exerting significant influence over health. Whether the influence actually exerted is negative or positive, it remains a concern of public health law. Public health law is as concerned with regulating the health degrading effects of the tobacco industry as it is the health benefiting effects of practices such as water fluoridation. Recognising the health-affecting conduct of State and non-State actors alike, public health laws impose responsibilities or obligations on range of governmental and non-governmental parties. For instance, public health law might seek to incentivise certain health-improving conduct on the part of private organisations or industry. In the United Kingdom for instance, the Soft Drinks Industry Levy, implemented by the 2016 United Kingdom Budget incentivized soft drinks manufacturers to reduce the sugar content of soft drinks, in an effort to tackle ever increasing rates of obesity.[19] Whilst some have derided the tax as a Pigouvian internalisation of the costs of obesity,

[18] Gostin (n2) 230.
[19] The Soft Drinks Industry Levy Regulations 2018.

the levy (or "sugar tax" as it is more widely referred to), has been successful in causing manufacturers to reduce the sugar content of products available to the public.[20]

Beyond incentivising conduct, governments partner with various different non-governmental institutions in order to fulfil public health objectives. The form that these partnerships take has been the subject of little study to date but, nonetheless, understanding the nature of the partnership between governments and non-governmental organisations is essential to public health law. In a study of public-non-governmental partnerships for public health, Martin Huskie found a number of different partnership models in operation in Ghana.[21] Ranging from contractual partnerships (i.e., the State contracting the work of the NGO) to 'equal' partnerships (i.e., collaborations between State and NGO sharing equal responsibility for securing outcomes), Hushie found that the legal form that the partnerships take affects the rate of attainment of the parties' shared objectives. This is perhaps unsurprising, given that different models of partnership prescribe the obligations of the parties with varying degrees of specificity and, further, only contractual models provide a legally enforceable obligation to discharge responsibilities. As such, public health law must identify those non-governmental partners with the ability to affect public health, whether positively or negatively, and seek to prescribe their privileges and duties in respect of public health. Furthermore, public health law has an interest in developing and establishing effective partnerships between parties in order to maximise impact.

In addition to the role of non-governmental partners, Gostin highlights the ever increasing role of private philanthropic organizations in securing public health. The Gates Foundation, and philanthropic organisations like it, play an ever-growing role in funding basic research into public health .[22] As such, philanthropy, through the funding of carefully selected research activities, has

[20] The British Soft Drinks Association reports at 26.8% reduction in the sugar content of soft drinks, following the introduction of the levy . See: http://www.britishsoftdrinks.com/Position-Statements/soft-drinks-tax
Last accessed 9th April 2019.
[21] Martin Hushie, 'Public-non-governmental organisation partnerships for health: an exploratory study with case studies from recent Ghanaian experience' (2016) BMC Public Health 963.
[22] Charlotte Tucker, 'Philanthropy Helping Public Health Achieve its Objectives: Donors Becoming Health Partners' (2014) The Nation's Health 1.

the ability to set or prescribe the research agenda within the academe and beyond. In this way, philanthropy plays an important role in prescribing the outer parameters of health affecting research.[23] The ability to regulate or control philanthropic financial aid and the consequent agenda setting is a developing concern of public health law. Both Gostin and the Institute of Medicine draw attention to the role of the academy in developing and deploying public health solutions, and the need for government agencies to incentivise and/or regulate certain research directions.[24] The rise of public health initiatives delivered by teams of academics and researchers rather than healthcare professionals can be attributed to a turn towards 'community-based participatory research', but the importance of philanthropic funding should not be understated.[25] Finally, Gostin highlights the transnational character of public health. Both public health problems and public health initiatives implicate a multi-agency approach, and one that oftentimes affects actors across borders. This facet of public health practice was perhaps most apparent in the international effort to control the 2013-2016 West African Ebola epidemic.

The need to appreciate a multi-agency approach is crucial to the safe and effective development and deployment of gene drive technologies. Current gene drive research involves a number of stakeholders: academic research institutions,[26] philanthropic funders,[27] target communities, and governments of the States within which target communities are located. The safe and effective deployment of gene drive technologies will require the involvement of further stakeholders. The establishment of an agency with responsibility for regulating gene drive research

[23] Devi Sridhar, 'Who Sets the Global Health Research Agenda? The Challenge of Multi-Bi Financing' (2012) PLoS Med e1001212.
[24] Institute of Medicine, The Future of the Public's Health in the 21st Century, (Washington, DC: The National Academies Press, 2003).
[25] For a helpful introduction to community-based participatory research, its challenges and methodologies, see: Andrea Cornwall and Rachel Jewkes, 'What is Participatory Research?' (1995) Social Science & Medicine 1667.
[26] In the United Kingdom, Imperal College London and the University of Edinburgh are pioneering gene drive research. See: --, 'Gene Drives for Vector Control' (*Imperial College London,* 2019) https://www.imperial.ac.uk/network-of-excellence-in-malaria/research/gene-drives-for-vector-control/ Last accessed 2nd May 2019; -- 'Gene Drive: Alternative Pest Control' (*University of Edinburgh,* 2019) https://www.ed.ac.uk/roslin/animal-genetic-engineering/research/gene-drive Last accessed 2nd May 2019.
[27] In the context of gene drive technologies specifically, almost all funding comes from philanthropy. In the United Kingdom, Imperial College's London's 'Target Malaria' initiative is almost solely funded by the Gate's Foundation. See: --, 'Who We Are' (*Target Malaria*, 2019) https://targetmalaria.org/who-we-are/ Last accessed 6th May 2019.

and deployment is an issue that will be returned to in later Chapters. Appreciating the multiplicity of players with the ability to exert control or influence over gene drive research and deployment is an important first step in disentangling complex questions regarding what party's privileges, obligations and duties ought to be within a regulatory framework. In respect of a number of challenges described above, public health law has not shied from identifying the range of relevant source agents, and instead places them explicitly within the constructed frame.

2.3.2 Limits on State Power & Source Agents

Governments can, and frequently do, exercise a range of powers in respect of population health. These powers vary in their nature – some are voluntary measures that aim to elicit health improvement by voluntary changes to citizen behaviour or business practices. These voluntary measures might comprise programmes of education, such as the UK Government's now well known '5 A Day' initiative encouraging citizens to increase their consumption of fruit and vegetables.[28] Alternatively, governments might pursue voluntary programmes by positively incentivising certain behaviours or practices.

What marks governments out from NGOs or concerned community groups, however, is their ability to *compel* health promoting behaviours or practices. Only governments can mandate the performance of certain actions or prohibit others. As Gostin puts it, "…government alone is authorized to require conformance with publicly established standards of conduct".[29] Examples of compulsory public health measures enacted by governments through law are numerous. Take, for example, the government's power to impose positive duties on private persons. In the United Kingdom there are laws that mandate citizens to wear seatbelts when travelling in cars or wear helmets when travelling on motorcycles[30] and there are laws that impose duties to disclose sexual

[28] For a media representation of the initiative, see: David Batty, 'Q&A: Five-a-day Campaign' (*The Guardian*, London, Monday 20th January 2003) https://www.theguardian.com/society/2003/jan/20/medicineandhealth.publichealth1 Last accessed 2nd May 2019.
[29] Gostin (n2) 9.
[30] The Motor Vehicles (Wearing of Seat Belts) Regulations 1993.

health status to sexual partners.[31] In addition to compelling private individuals, governments also impose positive obligations on private organisations in the pursuit of population health. The British Government, for example, has enacted laws obligating water supply companies to fluoridate the water they supply[32] and has required that manufacturers of tobacco package their products in a certain way.[33]

Not only do governments impose positive obligations on private persons and organisations, they also impose prohibitions upon them. In England and Wales, there are laws prohibiting individuals from smoking in public spaces.[34] In respect of private companies, there are laws that forbid the sale of alcohol to persons under the age of eighteen[35] and rules banning advertising by the tobacco industry.[36] Whilst promoting population health, all of these laws implicate other interests that liberal, pluralistic societies value. Requiring persons with HIV to disclose their sexual health status to unknowing sexual partners interferes with privacy rights provided for by the Human Rights Act.[37] Mandating the wearing of seat belts or motorcycles helmets, some argue, interferes with individuals freedom of choice, or autonomy interests.[38] Prohibiting the advertising of tobacco products demonstrably harms private economic interests.[39]

However, whilst health is a foundational value, it is not the sovereign virtue and where governments are faced with a particularly delicate balancing exercise, other values might triumph. The values that states might have to balance in the public health context are numerous. As demonstrated in the examples above, states might have to balance interests in health against environmental interests, health interests against autonomy interests, health interests against privacy

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[31] *R v Dica* [2004] EWCA Crim 1103.
[32] Water Industry Act 1991.
[33] Standardised Packaging of Tobacco Regulations 2015.
[34] The Health Act, s1(1).
[35] The Health Act 2006, s13.
[36] Tobacco Advertising and Promotion Act 2002.
[37] Matthew Weait, 'Criminal Law and the Sexual Transmission of HIV: R v Dica' (2005) Modern Law Review 121.
[38] David R Buchanan, 'Autonomy, Paternalism, and Justice: Ethical Priorities in Public Health' (2008) American Journal of Public Health 15.
[39] Kent M Lancaster & Alyse R Lancaster, 'The Economics of Tobacco Advertising: Spending, Demand, and the Effects of Bans' (2015) The International Journal of Advertising 41.

interests, health interests against economic interests, so on and so forth. Additionally, in proposing regulation to reduce any given risk to population health, states can cause an increase in another, ancillary population health risk. As such, states might also have to weigh one set of health interests against another set of different health interests. In this way, we begin to recognise that state powers in respect of public health are not without limits.

These complex balancing exercises play a significant role in limiting the regulatory options available to states. With regards to balancing health and economic interests, for example, not all state spending can be concentrated on health and, further, where public health regulations have sufficiently adverse economic consequences, they are eschewed by the state in favour of more cost-effective solutions. Similarly, where public health regulations interfere too greatly with the autonomy of their citizens, states reach for less invasive solutions. Thus, whilst states wield great powers in respect of health, those powers are not without limit. Such a conclusion is likely unsurprising from the standpoint of liberal, pluralistic democracies but it does provide a number of important insights into how public health problems are framed in law.

The first is that regulations imposing public health measures explicitly seek out and evaluate the range of values balanced against one and other. In part, it is public health law's ability to necessitate consideration of this broad range of values that ensures that the framing of the relevant problems is not constrained to examinations of safety to human health and the environment only. Secondly, asking questions about the limits of legitimate state intervention brings a wide range of potential target and source agents on screen – whether private individuals, private corporations, public sector institutions or NGOs – because it requires us to ask whose interests state powers affect.

Thus, as a part of the process of determining the limits of state power in the context of regulation, public health law does a good job of putting the relevant range of concerns associated with gene drive technologies into the frame. Asking questions about the limits of state power shines light on a range of practical concerns extending far beyond quantifiable harms to human

health and the environment, identifying the full range of actors implicated by the use of gene drive technologies.

2.4 Social Justice – The All Identifying Criterion

The discussion above associates the core commitments of public health law with the ability to identify overflows, target agents or source agents. However, public health law's commitment to social justice cannot be confined to any one of these three domains in respect of its ability to broaden frames. Instead, concern for social justice and the ethical enquiries it entails plays an important role in identifying overflows, target agents and source agents and therefore broadening the range of expertise and knowledge claims that we use to build our frames.

Although social justice is the seventh and final 'core concern' discussed in this survey of public health law's core commitments, many attest to its primacy. Gostin describes social justice as *the* core value of public health law.[40] Dan Beauchamp argues that that realisation of public health *is* the realisation of social justice, suggesting that social justice and a communitarian ethic are, and ought to be, the primary drivers of public health law.[41] Given the number of authors who trace the wellspring of contemporary public health ethics and public health law to debates arising out of legal responses to the HIV/AIDS crisis of the late 1980's and early 1990's, it is unsurprising that much of public health ethics, and therefore public health law, takes as its cornerstone concern for social justice.[42]

This section seeks to identify, quite briefly, what a social justice approach prescribes for public health law's approach to framing, before turning to the ways in which it is relevant to the regulation of gene drive technologies. In the first instance, a foundation in social justice broadly requires compliance with principles of distributive justice. Distributive justice requires states to act

[40] Gostin (n2) 21.
[41] Dan E Beauchamp, "Public Health as Social Justice" in *New Ethics for the Public's Health,* ed Dan E Beauchamp and Bonnie Steinbock (New York: Oxford University Press, 1999) 105–14.
[42] For a reflection on the role of the HIV/AIDS crisis in generating public health ethics and law with a commitment to social justice see: Nancy E Kass, 'Public Health Ethics: Foundations and Frameworks to Justice and Global Public Health' (2004) Journal of Law, Medicine and Ethics 232, 234-5; Madison Powers and Ruth Faden, *Social Justice: The Moral Foundations of Public Health and Health Policy* (Oxford University Press, 2008) Viii-Xii.

in order to ensure the fair allocation of public health benefits, but also to ensure the fair distribution of the burdens of interventions.[43] As such, when any public health measure, such as the release of gene drive technologies, is contemplated, regulators ought to take account of the distribution of the burdens it imposes. Whilst such an observation appears germane to any discussion of social justice, it reveals a further and invaluable insight that such an approach provides to public health law. Any approach rooted in social justice requires a careful mapping of the multiplicity of complex and interconnected pathways to inequality and disadvantage.

In this way, ethical enquiries play a substantive role in identifying the overflows that our frame ought to accommodate. Any framework embedding concern for social justice requires a conscious effort by legislators, policy makers and researchers to identify and explore these paths and consider how they might be affected, positively or otherwise, by the proposed public health measure. That is, to what extent are the range of existing structural disadvantages improved, or exacerbated, by the implementation of the proposed public health intervention? Similarly, such an approach requires pause to understand the ways in which existing disadvantage and inequality might affect the implementation and regulation of the proposed public health intervention. Put simply, states should ask whether existing social conditions or sources of inequality serve to complicate the roll out of any proposed intervention.

These considerations are particularly pertinent in the context of gene drive technologies. For example, a commitment to social justice requires regulators to identify the manner in which the benefits and burdens of a gene drive release might exacerbate existing inequalities. Further, and perhaps more importantly, commitment to the fair distribution of benefits and burden demands significant effort to identify the ways in which existing inequalities and disadvantage might hamper the safe and effective deployment of gene drive technologies. For instance, regulators ought to take account of cultural understandings or perceptions of genetic technologies.

[43] John Rawls, A Theory of Justice (Cambridge: Harvard University Press, 1971).

Strong social stigmas surrounding communities using gene drive technologies might further exacerbate limited access to healthcare or raise new socio-economic barriers. The devasting role of social stigma in worsening health outcomes for both individuals and populations – particularly in developing countries has been witnessed time and time again. In emergency responses to the Ebola virus in West Africa, fear and social stigma attaching to both the disease itself and the emergency response operation led to the abandonment of victims,[44] the murder of healthcare workers[45] and the further spread of the disease.[46] The fear-related behaviours that Shultz et al argue increased the spread of the disease and severely hampered the emergency public health response are, for the most part, symptoms of existing disadvantage and inequality.

If states and regulators are to take seriously their commitment to social justice, the cultural challenges posed to the safe and effective implementation of public health interventions must sit squarely within the frames we build in order to understand those interventions. Failing to do so negatively affects the safety, efficiency and efficacy of a proposed intervention, and therefore alters the distribution of the intervention's benefits and burdens. In instances where the distribution of benefits and burdens is altered so extensively as to render them unfair or inequitable, public health law places states under an obligation, grounded in the concern for social justice, to take steps to remedy the inequity, or where that cannot be achieved, seek out alternative solutions to the given public health problem.

In this way, the core commitments elucidated by Gostin invite an analysis of particular ethical, political and cultural questions – the answers to all of which tell us a little more about the phenomena that we are trying to understand and frame. In order to make sense of the wide range of implications that the introduction of a new technology or public health policy might have, these

[44] Mariam Davtyan, Brandon Brown & Morenike Oluwatoyin Folayan, 'Addressing Ebola-related Stigma: Lessons Learned from HIV/AIDS' (2014) Global Health Action 1.
[45] Mahammad Karamouzian and Celestin Hategekimana, 'Ebola Treatment and Prevention are not the only battles: Understanding Ebola-related fear and Stigma' (2015) International Journal of Health Policy and Management 55.
[46] Shultz et al, 'The Role of Fear-Related Behaviours in the 2013-2016 West Africa Ebola Virus Outbreak' 9 (2016) Current Psychiatry Reports 104.

core commitments require us to take account of a wide range of expertise – far beyond the technical – in order to construct the frame through which we understand it as a regulatory object.

3. Public Health Problems & Legal Responses

Having engaged in a theoretical discussion of the ways in which public health law builds broad frames, this section demonstrates, using two examples, how public health law achieves this in practice. I provide two case studies of public health laws from England and Wales. What develops below is a picture of system of legal responses developed from nuanced and robust framing of the problems they are drafted to tackle.

The two case studies from public health law's relatively short history presented below demonstrate its ability to provide innovative and effective legislative solutions, built from robust framing of the problems it faces. Part of this analysis entails noting the similarity between previous public health challenges or policies and those presented by gene drive technologies. Through these two short examples of Public Health legislation, we observe the ways in which lawyers have mandated the evaluation and scrutinization of a wide range of knowledge claims and expertise – particularly those that extend beyond the bounds of technical expertise alone. In this way, the reader is presented with example of lawyers exercising choice in the way the problems that they are confronted with are framed, or, in Fisher's words 'taking collective epistemic responsibility'.

3.1 The Sanitary Movement

The Sanitary Movement, led by Edwin Chadwick – social reformer, lawyer and close friend of Jeremy Bentham – oversaw the implementation of legislation recognising a State obligation in respect of its citizen health.[47] The suite of legislation enacted during the period that the sanitary movement was at its height reveals an interesting parable for lawyers and policy makers concerned with framing. What follows provides an analysis of framing failures and framing triumphs in public health law developed during and after the sanitary movement.

[47] For an excellent overview of Chadwick's ambitions and achievements and, indeed failings in respect of public health, see: Christopher Hamlin, *Public Health and Social Justice in the Age of Chadwick* (Cambridge, Cambridge University Press 1997).

3.1.1 The Public Health Problem

Edwin Chadwick's motivations for improving the sanitary conditions of England's poor were, in no small part, economic. At a time when the Elizabethan 'Poor Laws' were becoming increasingly unpopular and understood as a barrier to industrial and therefore economic growth, Chadwick's innovations aimed to reduce demand on poor relief.[48] Chadwick recognised that improving the living conditions of the poor would reduce the need for 'poor relief', in turn resulting in savings for the state.[49] One of the most profound ways in which the living conditions of the poor might be bettered was by improving sanitary conditions through the proper management and disposal of human waste and industrial effluent. As such, the development of an effective sewerage system was one of Chadwick's key aspirations.

After a number of Royal Commission reports and inquiries headed by Chadwick, 1848 saw the enactment of the first Public Health Act in England and Wales, along with a suite of accompanying Chadwickian legislation.[50] The Metropolitan Commission of Sewers Act 1848 appointed Chadwick Commissioner with responsibility for overseeing the development of sanitary systems. Furthermore, the Public Health Act 1848 established the General Board of Health (also headed by Chadwick) with responsibility for overseeing the improvement of sanitation and water supply in those towns with the worst health outcomes. The Act did this by establishing Local Boards with responsibility for the construction and maintenance of sewers, for building streets, and the provision of water supply.[51] The Local Boards, once established, remained accountable to the General Board of Health, who retained the power to interfere with the activities of the Local

[48] Peter M Solar, 'Poor Relief and English Economic Development before the Industrial Revolution' (1995) Economic History Review 1.
[49] See for instance: Edwin Chadwick, *Report to Her Majesty's Principal Secretary of State for the Home Department, from the Poor Law Commissioners, on an enquiry into the sanitary condition of the labouring population of Great Britain* (London: Clowes, 1842) and; Royal Commission for Inquiry into the State of Large Towns and Populous Districts (London: Clowes 1844).
[50] Public Health Act 1848. Related legislation included: Nuisances Removal and Diseases Prevention Act 1848; City of London Sewers Act 1848 and the Metropolitan Commission of Sewers Act 1848.
[51] Public Health Act 1848, s. X.

Boards, directing their programme of urban improvement and reprimanding them when necessary.[52]

A number of problems blighted the 1848 Act, so much so that it was quickly replaced by subsequent legislation.[53] In the first instance, the ethic of centralization or central government rule that the Act reflected was problematic both practically and politically. On a practical level, when inspectors appointed by the General Board were tasked with assessing the suitability of local measures, they tended to bring with them a 'one size fits all' approach and. in particular, one that subscribed to Chadwick's own, rather strong views on optimal sewerage solutions – pipe, rather than brick sewers.[54] This in turn lead to two further problems. The first was that approaches to sanitation fit for the particularities of a region were overlooked – for instance, little thought was given to local needs, including vulnerability to heavy storms and the potential for further growth in the area. As Christopher Hamlin suggests, on-site judgment capable of taking account of the nuances of a local situation were incompatible with Chadwick's agenda of centralization.[55] The second problem was that the pipe-sewers that the General Board were vociferous in their promotion of (until Chadwick's expulsion in 1854) were a subpar technical solution to the sanitation crisis.[56] The narrow gauge pipes of pipe sewer system regularly blocked and cracked, and furthermore were next to useless in the face of heavy storms. One notable civil engineer and contemporary of Chadwick complained that the General Board of Health had done:

> great evil… endeavoring to suggest general systems which were to prove panaceas, when the very nature of the work… required variations in levels, sizes of sewers' and materials not only varying with different localities, but also within each locality.[57]

[52] John Prest, *Liberty and Locality: Parliament, Permissive Legislation and Ratepayer's Democracies in the Nineteenth Century* (Oxford University Press 1990) 35.
[53] For example, Public Health Act 1856.
[54] Christopher Hamlin, 'Edwin Chadwick and the Engineers, 1842-1854: Systems and Antisystems in the Pipe-and-Brick Sewers War'(1992) Technology and Culture 680.
[55] Ibid 709.
[56] Lee Johnson, *Dirty Old London: The Victorian Fight Against Filth* (New Haven: Yale University Press 2014) 76-78.
[57] [Thomas Wicksteed] 'A Copy of a Report by Thomas Wicksteed, CE, On the State of the Works of Drainage and Sewerage in the Town of Croydon' PP, 1854 vol 61 (450) 5.

However, the problems confronting the 1848 Act were not only practical and technical, but political too. The centralization of power, authority and administration within the General Board of Health represented to some an unwelcome incursion into local government autonomy.[58] As John Prest notes, the Public Health Act was, at the time, widely considered Parliament's most profound sanctioning of State intervention in matters that had previously been the business of local government or private corporations.[59] As such, the Act was met with widespread political resistance from Victorian elites bearing considerable distrust for state paternalism.[60]

By 1852, a large enough portion of Chadwick's pipe sewers had been installed by the General Board in Croydon that assessments of their success might be made. Within weeks of the project's completion, the pipes of the sewer were broken and blocked and one tenth of Croydon's inhabitants had contracted typhoid.[61] Furthermore, the General Board's failure to navigate the tension between central government paternalism and local government autonomy rendered it impotent, ultimately leading to its abolition in 1858 by the new Public Health Act.[62]

With the end of Chadwick's tenure came the end of the dominance of the pipe sewer system of sanitation, and the brick sewers long advocated for by civil engineers became the common model. Furthermore, the legislation introduced over the following decade and a half delegated power and responsibility in respect of sanitation more completely to local government, thus overcoming concerns regarding the hegemony of central government.[63] As such, the legislation introduced following Chadwick's initial reforms was dogged by neither political resistance nor technical failings and, as a result, was significantly more successful in bringing about the objectives that Chadwick himself had been striving towards.

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[58]Dorothy Porter, *Health, Civilization and the State: A History of Public Health from Ancient to Modern Times* (Routledge 1998) 116.
[59] Prest (n52) 34.
[60] David Roberts, *Paternalism in Early Victorian England* (New Brunswick, Rutgers University Press 1979).
[61] See: Brian Lancaster, 'The "Croydon Case": Dirty Old Town to Model Town - The making of the Croydon Board of Health and the Croydon Typhoid Epidemic 1852-53,' Croydon, Croydon Natural History and Scientific Society, Published by the Croydon Natural History and Scientific Society, 2001, vol18 (7) 145-206.
[62] The Public Health Act 1852. For a wonderfully illustrative descriptive of challenges of the era see: Porter (n58) 126.
[63] Local Government Act 1858 and Public Health Act 1875.

Social historians have tended to attribute the collapse of the first Public Health Act and the comparative success of its descendants to either political or technological causes. Both Samuel Finer and Richard Lewis have favoured political explanations for the Act's failings, whilst Christopher Hamlin has suggested that technical misunderstandings likely played the biggest role in the Act's downfall.[64] However, there is a third way in which we might understand the relative lack of success attained by Chadwick's legislative approach – a failure of framing.

Chadwick's failure was not one of either political or technical error, but a mistake in both domains that flowed from a failure of framing, insofar as he failed to properly understand both the problem he sought to tackle and the implications of the solutions that he favoured – a system of pipe sewers developed and overseen by a central administration. That Chadwick's failure was indeed one of framing is perhaps most obvious when we consider Christopher Hamlin's description of the situation that confronted Chadwick:

> Facts were in dispute; was there really mud in certain sewers? How fast did a sewer of given design discharge a given amount of water? There were also conflicts about the nature of expertise, the proper institutional and social framework for sewerage projects, and what constituted success and failure? The two sides even disagreed what they were disagreeing about.[65]

Put differently, Chadwick was confronted with what Callon might call a 'hot situation' in need of framing.[66] What overflows existed and how those overflows might be measured was not yet agreed, nor was the identity of source and target agents affected by both the problem or its proposed solutions.

Ultimately, much like the pipe sewers he advocated for, the frame that Chadwick adopted was too narrow for the task in hand. The overflows that Chadwick's technical and legislative approach overlooked ranged from the effects of heavy storms, town growth, human error and political resistance. Some of Chadwick's myopia is perhaps attributable to his concern for economic improvement. The overflows that Chadwick was concerned to identify were economic

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[64] Samuel E Finer, The life and Times of Sir Edwin Chadwick (London: Methuen 1952) 439-452; Richard A Lewis, Edwin Chadwick and the Public Health Movement 1832-1854 (London: Longmans, Green & Co. 1952) 222-223.
[65] Hamlin (n54) 681.
[66] Michel Callon, An Essay on Framing and Overflowing: Economic Externalities Revisited (1998) The Sociological Review 244.

Were pipe sewers more or less expensive than brick sewers? How much could the state save? As such, Chadwick's conception of the relevant overflows, as well as his measure of success, were constrained by economic considerations.

Instead of asking whether pipe-sewers were capable of withstanding heavy rain or surges in throughput, Chadwick asked how much they might cost, and how much they might save.[67] Instead of asking whether central administration might be met with resistance, or even be administratively unworkable, Chadwick considered the savings that might be made by a centralised and generalised system. As Knut Ringen suggests, Chadwick's tendency to reduce all evaluations to entries on a balance sheet can, more broadly, be attributed to Chadwick's utilitarian proclivities.[68]

Seeing the failings of Chadwick's approach, the laws that followed provided solutions for the overflows that Chadwick overlooked. The Metropolis Management Act 1855 repealed the Metropolis Commission of Sewers Act 1848, abolishing the Chadwickian Commission and replacing it with the Metropolis Board of Works.[69] Joseph Bazalgette was appointed Chief Engineer of the Board, ensuring the end of pipe sewer systems and the development of the more effective brick sewers instead.[70] Thus the overflows unaccounted for by Chadwick's technological approach were now accommodated by Bazalgette's concerns. Furthermore, the Public Health Act 1858 abolished the General Board of Health and, along with the Local Government Act of the same year, local boards were granted additional powers free from the fetters of a central authority.[71] In this way, the succeeding legislation avoided the political resistance that had rendered the General Board of Health impotent in improving sanitary conditions across the country.

This brief rehearsal of the legislation enacted by the Sanitary movement highlights a number of salient features of both a 'public health problem' and, further, what is required for effective

[67] General Board of Health, 'Minutes of Information Collected with Reference to Works for the Removal of Soil Water or Drainage of Dwelling Houses and for the Sewerage and Cleansing of the Sites of Towns' PP 1852 vol 19 98.
[68] Knut Ringen, 'Edwin Chadwick, the Market Ideology, and Sanitary Reform: On the Nature of the 19th-Century Public Health Movement' (1979) International Journal of Health Services 107.
[69] Metropolis Management Act 1855; Metropolis Commission of Sewers Act 1848.
[70] Johnson (n56) 89.
[71] Public Health Act 1858; Local Government Act 1858.

legislative solutions. In the first instance, public health problems sometimes necessitate ambitious changes to the environment or the conditions in which people live. Secondly, there often exist tensions between autonomy (both individual and institutional) and paternalism.

Effective legal responses to these particular challenges often require reforms of institutional responsibilities, supported by settled political structures with strong government backed by regional or devolved decision makers and infrastructure. We will return to these lessons and their particular relevance to the regulation of gene drive technologies later.

3.2 Water Fluoridation Legislation

The second historical illustration of public health laws taken up here concerns water fluoridation. Since the 1960s, various governments within the British Isles have instituted water fluoridation legislation. Programmes of water fluoridation are pursued in order to reduce the incidence of dental caries within the population, and thus improve oral health.[72] Despite this laudable aim, as the discussion below demonstrates, the road to fluoridating water supplies in the United Kingdom has been far from straight, and in some places, has never led anywhere at all. The challenges faced by any attempt to regulate the fluoridation of water are three-fold. Firstly, objectors to fluoridation cite concerns regarding the safety of fluoridated water.[73] As such, legislators are charged with taking account of citizen concerns for bodily integrity where they fear harm might follow the ingestion of fluoridated water. Secondly, water supplies (like mosquitos) criss-cross political boundaries. Water suppliers charged with fluoridating water supplies serve multiple local authority areas and, as such, the decision of one local authority to fluoridate water for its citizens effects neighbouring local authorities and their citizens. Thirdly, some object to water fluoridation programmes because of their purported interference with autonomy interests. The claim made by dissenters is that the fluoridation of water supplies against the wishes of community members constitutes an unjustified

[72] - - 'Water Fluoridation: Health Monitoring Report for England 2018' (Public Health England, 2018) https://www.gov.uk/government/publications/water-fluoridation-health-monitoring-report-for-england-2018 Last accessed 2nd May 2019.
[73] M McNally and J Downie, 'The Ethics of Water Fluoridation' (2000) J Can Dent Assoc 592.

interference with autonomy and freedom of choice. What is impressive about what might otherwise be considered a particularly mundane piece of legislation, is that the framing of the problem picks up and responds to the full range of complexity.

The legal history of Water Fluoridation in the United Kingdom demonstrates well the attempts of legislators and judges to grapple with and resolve all three of the problems described above and it is to those legal developments that we now turn. In England and Wales, the legal basis for water fluoridation can be found in the Water Industry Act 1991, as amended.[74] Section 87 of the Act imposes on water suppliers a duty to fluoridate water supplies when requested to do so by the relevant authority. Following the Health and Social Care Act 2012, 'relevant authority' is defined as a county council, or, where there is no county council, the district council.[75] The following four sections of the 1991 Act (87A-88A), provide for the technical aspects of the undertaking, such as the concentrations of fluorine that ought to be attained, and arrangements around complying with and varying the duties imposed.

With respect to the first overflow articulated above – concerns about the safety of fluoridated water and therefore bodily integrity – the legislation imposes obligations on local authorities. The statutory obligations to review and monitor the safety of fluoridation are the most obvious instantiation of respect for this concern by legislators. The regular regional review of the health effects of fluoridation ensures the continued safety of water fluoridation, whilst continuing to gather data regarding the long-term risks and benefits of such an intervention. Section 90A requires local authorities to mount a review of their fluoridation protocol and its effects within four years of the start of fluoridation, and every four years after that.[76]

Secondly, the legislation accommodates *all* of the relevant target agents. One of the challenges of legislating for water fluoridation is that any programme of water fluoridation

[74] Note the Water Act 2003 and various statutory instruments, change the identity of the authority with whom this power to fluoridate the water supplies are vested. This has little practical effect but rather just reflects broad changes in the institutional character of those agencies vested with responsibility for healthcare provision.
[75] Health and Social Care Act 2012, s 5.
[76] Water Industry Act 1991, s90A(3)-(4).

implicates multiple local authority decision makers across a large geographical area and with varying population demographics. In order to resolve difficulties surrounding the fluoridation of water supplies serving multiple local authorities, some of whom may not welcome fluoridation, the Act also provides for a joint committee procedure. This joint committee procedure aims to provide for a collaborative decision-making process, capable of taking account of and weighing the views of the different local authorities. The local authority drawing up the initial fluoridation proposal must notify all affected local authorities and establish a joint committee.[77] All subsequent decision making on the proposal happens through the joint committee, with each local authority having a single block vote, the size of which is determined by reference to the proportion of total individuals affected residing within that local authority area.[78] Only proposals securing over 67% of the total block vote succeed.[79]

As such, the way that the challenges posed by fluoridating shared water supplies were framed did not shy away from the complexity associated with identifying the vast range of target agents affected. Instead, all possible target agents were included within the frame, and a legal procedure through which those agents might articulate their interests was drawn up.

In this way, public health law demonstrates its ability to legislate for difficulties surrounding decisions capable of binding multiple administrative jurisdictions or, in other words, a range of target agents or populations, each with varying interests. This particular insight will be returned to in the penultimate Chapter of the thesis, but it is helpful to raise the relevance of this procedure to regulation of gene drive technologies here. Gene drive organisms, like water supplies, will cross political and jurisdictional boundaries once released because they cannot be effectively confined to or contained within a particular geographical area. Due to the lack of spatial confinement of modified insect populations, a co-operative and collaborative decision-making procedure between

[77] Water Industry Act 1991 s88E(5).
[78] The Water Fluoridation (Proposals and Consultation) (England)Regulations 2013 7(4)(b).
[79] The Water Fluoridation (Proposals and Consultation) (England)Regulations 2013 7(3).

the community proposing a gene drive release and its affected neighbours will be essential to the safe and effective use of the technology.

Finally, the legislation has faced and, to some extent, overcome challenges associated with another overflow – purported violations of citizens autonomy interests. Section 89 of the 1991 Act imposes on the local authority an obligation to engage in a public consultation process, prior to implementing a programme of fluoridation.[80] Section 5 of the Water Fluoridation (Proposal and Consultation) (England) Regulations 2013 further elaborates on the obligations of the local authority with regard to the consultation process, placing substantive requirements on publicising the proposal and establishing a mechanism by which affected parties might raise their concerns.[81]

The 2013 Regulations repeal the Water Fluoridation (Consultation) (England) Regulations 2005, which said significantly less about the consultation process and how it ought to be taken account of when making final decisions about a proposal for fluoridation.[82] Significantly, the consultation process in section 5 and the 'decision-making process' prescribed by section 6 of the 2013 Regulations were, in part, a response by legislators to *Milner v SHA [2011].*[83] Milner sought judicial review proceedings of the South Central Strategic Health Authority's decision to fluoridate the water following public consultation. There had been 10,000 respondents to the consultation, representing the views of approximately 5% of the affected population. Of the 10,000 respondents, over 72% objected to the fluoridation of their water supply.[84] As such, a clear majority of those responding to the public consultation did not support the proposal and Milner sought to argue that in the absence of majority support, the strategic health authority's decision to continue with the fluoridation proposal was unlawful. In deciding against the claimant, Justice Holman in the High Court described the legal position as follows:

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[80] Water Industry Act 1991, s 89.
[81] The Water Fluoridation (Proposals and Consultation) (England)Regulations 2013, s11.
[82] Water Fluoridation (Consultation) (England) Regulations 2005.
[83] See: Explanatory Memorandum to The Water Fluoridation (Proposals and Consultation) (England) Regulations 2013 [2013 No.301] https://www.legislation.gov.uk/uksi/2013/301/pdfs/uksiem_20130301_en.pdf. Last accessed 16th April 2019.
[84] See *R (on the application of Milner) v Southampton Strategic Health Authority* [2011] EWHC 218 (Admin).

> Contrary perhaps to the belief of Ms. Milner and others, it is not the law that fluoridation can only occur when a majority of the local population agree… The SHA have not acted unlawfully, and no court can interfere with their decision.[85]

In effect, the 2013 Regulations put Justice Holman's pronouncement of the law on a statutory footing, with the explanatory memorandum accompanying the Regulations stating explicitly the government's view that "decisions on fluoridation proposals should not be determined solely by a count of the representations received, or by local referendums".[86] Section 6 provides for a final decision making process, requiring the local authority to take into account the extent of public support, the strength of scientific and ethical evidence and the capital and operating costs associated with implementing the proposal.[87] As such, whilst community opinion is taken account of, it is not determinative of the decisions to fluoridate. Thus, the 2013 Regulations place the competing values of autonomy and health within the frame through which we understand the implications of fluoridating shared water supplies. Critiques of the Act and the accompanying regulations argue that the public consultation process is toothless, doing little to protect citizens autonomy interests and instead only paying lip-service to them.[88] Such a view however, places a burden on the concept of autonomy that it is not fit to bear, in effect making it the sovereign value, trumping all other interests whenever a conflict does emerge. With respect to the ways in which we frame new technologies and the challenges that they present us with, what is perhaps most exciting about the Water Fluoridation Regulations is that they identify no sovereign voice or value when it comes to making decisions about whether or not any given supply of water should be fluoridated. They eschew both the hegemony of technical expertise and the tyranny of autonomy, instead providing clear guidance on the range of knowledge claims that ought to be taken account of and scrutinized in making these decisions. They explicitly require that the current scientific

[85] See *R (on the application of Milner) v Southampton Strategic Health Authority* [2011] EWHC 218 (Admin) [86].
[86] See: Explanatory Memorandum to The Water Fluoridation (Proposals and Consultation) (England) Regulations 2013 [2013 No.301] 7.2. https://www.legislation.gov.uk/uksi/2013/301/pdfs/uksiem_20130301_en.pdf. Last accessed 16th April 2019.
[87] The Water Fluoridation (Proposals and Consultation) (England)Regulations 2013, s6.
[88] David Shaw, 'Weeping and Wailing and Gnashing of Teeth: The Legal Fiction of Water Fluoridation' (2012) Medical Law International 11, 16.

evidence be scrutinized and regularly reviewed and updated.[89] Public opinion has to be taken account of, and a legal procedure by which this might be achieved is laid out.[90] Local authorities are required to consider whether current or future infrastructures can cope with the alterations that implementing water fluoridation would require and consideration of the economic benefit and burden are required too.

As such, the discussion above highlights the ways in which public health law places a range of complexities within the frame it builds for understanding water fluoridation and its potential implications. In this way, public health law acknowledges and navigates the tensions between population health and autonomy, between issues of science and value. Decision making under the Act is not determined by either technological determinism or public participation alone. Instead, the Act explicitly requires decision-makers take into account a range of factors, asking questions about the available scientific evidence, public opinion, economic viability and administrative feasibility.

Thus, these examples tell us a number of things about public health – and many of those things are relevant to the regulation of gene drive technology. The first, is that there is almost always tension between the exercise of State power and individual liberty, local authority powers or, increasingly in the era of 'New Public Health', the freedoms of private organisations.[91] All of the legislation we have surveyed stands in need of justification for incursion into any of those fields of autonomy. Precisely the form that the required justification takes is a matter of some variance, but we will return to this shortly. Secondly, and relatedly, public health law requires certain State infrastructure. Even where the exercise of State power is theoretically justified, the policies legislated for cannot succeed in their aims in the absence of sufficient institutional support and

[89] The Water Fluoridation (Proposals and Consultation) (England)Regulations 2013, s6.
[90] Ibid.
[91] New Public Health refers to strand of publc health activities concerned with modifying the behaviour and lifestyle of person, considered in opposition to 'old public health' which was more concerned with altering the conditions and environments in which people lived. For perhaps the most comprehensive overview, see: Theodor H Tulchinsky and Elena A Varavikova, *The New Public Health* (San Diego: Elsevier, 3rd edn 2014).

administration. Thirdly, it becomes clear that public health law implicates a wide range of stakeholders, decision-makers and beneficiaries.

4. Conclusion

This Chapter has sought to demonstrate that lawyers can and do build robust frames for the problems that they are drafted in to tackle. In areas of high complexity, regulatory decision-making need not be dominated by technical expertise alone. Instead, lawyers can and do scrutinize a wide variety of expertise, knowledge claims and values in building the frames within which they understand new technologies as regulatory objects.

Chapter Four went some way to suggest that the GMO regime, due to the way it frames GM technologies, focuses almost exclusively on quantifiable risks to human health and the environment and therefore on scientific findings and technical expertise alone. The unfortunate consequence of a focus on scientific determinations of safety in respect of human health and the environment when building our frames of understanding, is the way in which it strips the decision-making process of questions of value. To be sure, not all consider denuding regulatory decision-making of value judgements to be a bad thing – as suggested in Chapter One, some technologies might be adequately regulated by reference to technical expertise alone. However, this thesis argues that decision-making around the regulation of gene drive technologies *is* inherently value laden. Whether we decide to authorize or deny certain uses of gene drive technologies rests on a series of complex value judgements which have implications for the way we live in the world.

Once gene drive technologies are properly understood and framed, it is clear that questions about how they ought to be regulated implicate questions about the world we choose to build and the world in which we want to live. What the analysis of public health law in this chapter has demonstrated is that we, as lawyers, are capable of building frames and regulatory regimes that acknowledge and respond to all of the complexities of a given problem, incorporating both technical expertise and questions of value. Whilst scientific assessment of the risks any proposed measure poses to human health (or the environment) remain important, they are accompanied by

self-avowedly ethical and political determinations of the measure's merit. Value judgments and political enquiries populate many of the 'core concerns' identified by Gostin and were demonstrated in practice by the two legislative examples proffered above. In part, this is because we recognise that public health law implicates a trade-off between a multiplicity of goods valued by liberal, pluralistic societies.

This is not to say that public health law is capable of providing all the answers to how we might best regulate gene drive technologies. The analysis developed here is, perhaps, exploratory rather than prescriptive. My aim is to suggest that we have choices to make in the ways that we think about technologies and how best to regulate them, and that public health law offers an example of a discipline with a history of making good choices.

CHAPTER SIX: ENVIRONMENTAL ETHICS OF GENE DRIVE TECHNOLOGIES

Chapter by chapter this thesis has been building an argument that demands lawyers think carefully about how they understand and frame the technologies that they are tasked with regulating. Having, in Chapters One to Four, demonstrated the inadequacy of understandings and frames built almost exclusively on technical expertise, the last chapter began to consider how frames might be broadened, discussing the ways in which the social, political, cultural and ethical implications of a technology might be subjected to regulatory scrutiny. This Chapter focuses on the role that substantive ethical enquiry might play in broadening out the frames that we build, so as to ensure that they bear fidelity to the realities of the technologies that we seek to regulate.

This chapter does two things. In the first instance, it offers a working out of some aspects of the ethical qualities of gene drive technologies. Given the relative nascency of the technology such an analysis has yet to be developed within the literature. Secondly, I highlight the ways in which the ethical questions posed below might play a role in bridging some of the epistemic gaps presented by gene drive technologies. In this way, I propose that ethical enquiry can help articulate some of the questions that scientific and technical experts need to answer if we are to be sure that the use of gene drive technologies is both safe and fair. That is, ethical enquiry aids lawyers in taking collective epistemic responsibility by identifying the knowledge claims relevant and necessary for the construction of reliable frames.

Throughout this Chapter, I highlight the overflows and populations of target agents that ethical enquiry puts on screen – overflows and target agents that go overlooked when we construct our frames with technical expertise alone. Ultimately, I demonstrate that asking questions about the ethical qualities of our proposed uses of technology is vital to building robust regulatory frames.

The Chapter breaks down into two sections. The first considers the ethics of eliminating entire species or, in other words, the ethics of population suppression drives. In essence, the

question is whether there can be sustainable moral objections to eliminating entire species in the absence of harm to any individual of the species concerned. These ethical questions relate directly to issues that might arise in the context of a population suppression drive. I will address in turn the contributions made by Ronald Sandler, Charles Foster and Larry Johnson, before settling on the moral inconsiderability of species. Whilst I settle on the moral inconsiderability of species *per se*, the analysis that reaching any conclusion necessarily entails identifying a range of concerns that regulators ought to be cognizant of on a case by case basis, and the overflows that ought to make it into the frame.

The second section asks whether there is any ethical impediment to changing or replacing the characteristics of a species at the population level. In other places, this kind of intervention has been referred to as 'sculpting evolution' or, at the very least, directed evolution.[1] In many ways, humans have been engaged in directing the evolution of a multiplicity of species for many centuries and have done so through selective breeding. This section will ask whether gene drive is sufficiently different to selective breeding to trigger novel moral concerns. As such, Section Two pertains most directly to the ethics of population alteration drives.

Finally, in drawing some broad conclusions regarding the ethics of certain types of gene drive and their proposed uses, I consider how this ethical enquiry might inform the ways in which we go about thinking about gene drive technologies for the purposes of regulation. One of the primary purposes of this Chapter is to assess whether gene drive technologies present any *intrinsic* moral concerns that might provide cause to prohibit their use, that is, whether there are any moral concerns that are not contingent on the specific use to which the technology is put. However, this Chapter also serves as a demonstration of the way in which ethical questions can illuminate regulatory framing.

[1] Kevin Esvelt, 'Engineering Biology in light of Evolution' (*Sculpting Evolution,* 2019) http://www.sculptingevolution.org Last accessed Sunday 14th April 2018.

1. Ethics of Species Elimination

Gene drive technologies present us with the option of rapidly and completely eradicating the species that we deploy them in. As such, it behoves us to ask whether the eradication of entire species is ethically permissible.

1.1 Ethical Value of Individual Gene Drive Organisms

In contemporary bioethics, it is relatively uncontroversial to assert that some non-human individuals are morally significant and thus we owe them certain duties or forms of protection. Some theorists, if not most, assign this moral significance on the basis of properties or traits possessed by the individual in question. Since Bentham, sentience has regularly been considered one of those properties; by virtue of a creature's capacity for suffering we owe it moral consideration.[2] Other theorists have set the bar somewhat higher, requiring evidence of higher cognition before recognising non-human animals as members of the moral community. Clifford Grobstein, for example, lays down three criteria: firstly, 'behaviour diagnostic of a rudimentary self-state', for example, the ability to respond to external stimuli; secondly, 'possession of non-behavioural functional processes', where Grobstein requires that a being can be recognised as a self by others; finally, Grobstein requires that in order for a being to be ascribed moral status it ought to have the ability to evoke empathy as another self.[3] In this way, Grobstein sets the bar reasonably high, requiring high level cognition and particular social pre-conditions for ascriptions of moral status. On Grobstein's account, only human beings and a handful of animal species find themselves within the sphere of moral considerability. At the opposite end of the spectrum, Kenneth Goodpaster has argued that the mere display of biological life might be sufficient for the instantiation of moral significance.[4] Thus, Goodpaster might attribute interests and therefore some moral significance to plants and all animal life, whilst such attributions are not permitted by Bentham or Grobstein's theories.

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[2] Jeremy Bentham, An Introduction to the Principles of Morals and Legislation (Oxford: Clarendon Press 1907).
[3] Clifford Grobstein, Science and the Unborn: Choosing Human Futures (New York Basic Books, 1988) 62.
[4] K E Goodpaster, 'On Being Morally Considerable' (1978) The Journal of Philosophy 75(6), 320.

To say an individual is morally significant or has 'moral status' is not to say that it is inviolable, but at the very least suggests that the individual should not be harmed without sufficient justification. In guiding our own actions as moral agents, we must take into account the interests of fellow members of the moral community. Whether we consider moral significance to be scalar or a threshold concept, it exists as a matter of degree. Thus, whilst owing to an elephant's sentience we might consider it morally significant on the capacity-based view, the interests of higher life (humans being the most obvious example) will likely trump the interests of the giant pachyderm. Equally, we have few reservations about ridding our pets of worm infestations by the use of helminthicides that kill off individual parasites because we recognise, at least in part, the greater suffering and thus moral significance of the dog as compared to that of the insect pest. In these cases, assessing the moral significance of the individuals and ascertaining the correct balance is straightforward. Whilst troublesome marginal cases do exist, such cases are of little concern here.[5]

Proceeding on this basis, we can quite sensibly ask whether insect vectors are morally significant. Do we consider individual *Anopheles Gambiae* members of our moral community? Little evidence exists regarding insect capacity for suffering, but what is known suggests mosquitos are far from what we ordinarily consider sentient and even further still from possessing any of the sorts of traits that a theorist such as Grobstein requires for attributions of moral status. As such we can say with some confidence that individual mosquitos (and insect vectors more generally) lack moral significance and, as such, are not members of our moral community. Further, we might even have good reason to argue that there is a negative value in the existence of mosquito species, insofar as they play no discernible role in their ecological niche whilst being one of the most abundant disease vectors.

In any case, oftentimes in the gene drive context (and certainly with regard to population suppression drives), the moral significance of the target individuals fails to be a relevant

[5] For instance, see 'The Einstein Problem' in Stephen W Smith, End –of-Life Decisions in Medical Care: Principles and Policies for End of Life Decision Making (Cambridge University Press 2012) 35-38.

consideration. Gene drives such as the one proposed by Hammond *et al* do not kill individual insects but rather determine the biological sex of their progeny. During its own lifespan the individual mosquito will suffer no harm as a result of its engineered genome. It is in this way that gene drive technologies are often considered a more humane population control tool than current alternatives. Certainly, gene drive technologies appear to be a cleaner and more efficient solution than physical or chemical pest control techniques such as traps or poisons. Thus, questions of harm and related questions of moral significance fail to arise.[6] Aside from the fact that we do not in the first instance attribute moral significance to mosquitoes, as far as we are currently able to understand, genetically determining the biological sex of an individual insect does not cause it any harm or frustration of its individual interests. As such, whilst in theory a suppression drive might eliminate an entire species, it does so without harming any individual member of that species. Therefore, the questions raised here are quite different – instead of considering the moral significance of the individual, it is the moral significance of the *species* that matters. If there are to be any sustainable moral objections to species eliminating population suppression drives, they must claim that species as a concept is capable of holding interests.

To be sure, interest-holding alone is not the only way in which some general or moral obligation to preserve a thing might be instantiated. As Notre Dame burned, few would dispute that it's diminishment by flames was to be lamented. As an arrangement of bricks, wood and mortar, the cathedral itself could not be said to be capable of holding interests but, nonetheless, we consider it a thing of value, so much so that we ought to take measures to ensure its preservation. In *Life's Dominion*, Ronald Dworkin articulates these phenomena as representations of intrinsic value.[7] Dworkin describes the ways in which the ways in which we value things can vary. We can value things *subjectively*, *instrumentally* or *intrinsically* – and where we value them intrinsically, there is, according to Dworkin, at least a presumption that they ought to be protected,

[6] Hammond and others, 'A CRISPR-Cas9 Gene Drive System Targeting Female Reproduction in the Malaria Mosquito Vector Anopheles Gambiae' (2016) Nature Biotechnology 78.
[7] Ronald Dworkin, Life's Dominion: An Argument about Abortion and Euthanasia (Harper Collins 1993) 71-74.

preserved and maintained. As examples of non-interest holding, but intrinsically valuable entities, Dworkin provides sculptures, works of art, dying languages and endangered animal species.[8] Speaking directly to the intrinsic value of species, Dworkin says:

> We think it very important and worth considerable economic expense, to protect endangered species from destruction at human hands or by a human enterprise—a market in rhino tusks, valued for their supposed aphrodisiac power; dams that threaten the only habitat of a certain species of fish; or timbering practices that will destroy the last horned owls. We are upset—it would be terrible if the rhinoceros ceased to exist—and we are indignant: surely it is wrong to allow such a catastrophe just so that human beings can make more money or increase their power.[9]

Dworkin concludes that we know species to have intrinsic value for reasons other than our ability to experience their existence, and instead because 'we think it would be a shame if human acts and decisions caused them to disappear'.[10]

However, whilst these sorts of attitudes exist in respect of horned owls and white rhinos, they are not universal to either all species or, furthermore, all instances of potential extinction. As Lily May Russow points out – we struggle to point to value, much less any intrinsic value, in respect of many other species.[11] That we do not attribute *all* species intrinsic value is plain when we consider that the global eradication of the small pox virus,[12] or the New World Screw Worm[13] failed to elicit the same moral attitudes. As such, we should be dubious of the claim that all species possess intrinsic value and that each and every species that blinks into non-existence is cause for lamentation or regret.

Instead, what Dworkin's commentary reflects is less about the value of species *per se*, but our attitudes towards the circumstances of their extinction. It is the quality of the 'human acts and decisions' that brings them to extinction that stirs upset, outrage and indignation rather than sustained reflection on their intrinsic value. It is our disgust that the white rhino loses out to the

[8] Ibid 72.
[9] Ibid 75.
[10] Ibid 75.
[11] Lily May Russow, 'Why Do Species Matter?' (1981) Environmental Ethics 101, 103.
[12] World Health Organisation, The Global Eradication of Smallpox: Final Report of the Global Commission for the Certification of Smallpox Eradication (Geneva, WHO 1979).
[13] For a discussion of the eradication of New World Screw Worm, see the introduction to: A P Gutierrez, L Ponti and P A Arias, 'Deconstructing the Eradication of New World Screwworm in North America: Retrospective Analysis and Climate Warming Effects' (2019) Medical and Veterinary Entomology 282.

absurd belief that it's horn might instantiate desire, lust and virility. It is our regret that the horned owl loses out to human practices driven by greed and want of profit. Having ruled out the claim that *all* species possess intrinsic value capable of grounding their moral considerability, I turn to ask whether species are capable of holding interests that might ground their moral considerability instead.

1.2 Ethical Value of Species

Whether species are capable of possessing interests, and therefore whether they can be attributed with moral significance, has been a matter of some debate within the field of Environmental Ethics. Broadly speaking, the debate is split into two camps: those who assign moral significance to whole species, and those who do not. However, each theorist reaches their conclusion via a different route and, as such, there is no methodological consensus as to how the question might be approached. Before we proceed to evaluate the arguments that have gone before, it is worth noting that when we talk about 'whole species', we are referring to species as a concept.

Organising the arguments of those who do and those who do not support ascriptions of moral significance to whole species is no straightforward task. Ronald Sandler attempts to make sense of the literature by offering what he calls a 'typology of value', categorising and critiquing the different arguments.[14] Sandler splits the literature into arguments from instrumental value, subjective value and objective value. With regard to objective value, Sandler then divides the arguments into two further categories – those arguing for natural historical value and others arguing for inherent worth. Ultimately, Sandler contends that arguments from objective value are unable to account for the moral considerability of species, but that in certain instances we might attribute subjective or instrumental value to a species and, where we do so, we can say that certain species *are* morally considerable.[15]

[14] Ronald L Sandler, *The Ethics of Species: An Introduction* (Cambridge University Press 2012) 16-20.
[15] Ibid 46.

Whilst Sandler's approach is a plausible one, it is not without its pitfalls. Sandler's treatment of instrumental and subjective value is located at the individual rather than species level and therefore the account that he provides cannot be said to be an account of the moral considerability of *species*. Rather, he offers an account of the moral considerability of *certain* species. The conclusion that the instrumental value of species must be assessed on a case-by-case basis entails an assessment of the instrumental value of traits of individuals, writ large.[16] To say, as Sandler does, that we assign instrumental value to the horseshoe crab species for its medicinal properties or to honey bee species for their honey making focuses on the individual, or an aggregation of the individual, not the species itself as a concept. Similarly, to say that the subjective value of the tiger species is rooted in aesthetics draws the argument down from the species level to that of the individual.[17] As such, in the absence of the instrumental value of individuals (such as is the case with mosquitos), there can be no ascription of moral significance to species. Sandler is not therefore making an argument for the moral considerability of species, but rather, the moral considerability of *a* species.

Such a move is not uncommon within the literature and Sandler is far from the only offender.[18] However, if it is possible to establish the moral significance of species, we must conceive of it as something other than a grouping of individuals, given that gene drive technologies do not bear implications for individual members of a species. At this juncture then, it helps to split the debate somewhat differently to Sandler and instead divide the arguments along the lines of individualists and holists. Individualists consider only individual, sentient beings capable of holding interests and therefore only sentient individuals qualify as morally considerable patients.[19] Holists,

[16] Ibid 23.
[17] Ibid 24.
[18] Kristin Shrader-Frechette, 'Individualism, Holism and Environmental Ethics' (1996) Ethics and the Environment 1(1) 55
[19] Joel Feinberg, 'The Rights of Animals and Unborn Generations' in W T Blackstone (Ed) *Philosophy and Environmental Crisis* (University of Georgia Press 1974, 43.

on the other hand, consider that complex systems can be considered entities or wholes, morally relevant in their own right, and more than just a collection of their parts.[20]

Viewed this way, Sandler is very much an individualist who, unlike his holist counterparts, considers species to be constituted as a class comprised of individual members – that is, he adopts a class conception of species. Sandler's use of the class concept, sometimes referred to by others as a natural kind concept, reflects the framework adopted by Carl Linnaeus in his development of an early taxonomy for the natural world.[21] The classical theory of concepts understands a class concept as prescribing a body of knowledge about which properties are separately necessary and jointly sufficient in order for inclusion within the class.[22] Class concepts then, function as definitions. Thus, Sandler understands the *panther tigris* species (or any other species for that matter) as a group of individuals with properties both necessary and sufficient for inclusion within the definitional class *Panther tigris*. In light of the class conception of species, it is difficult to suppose how a group of individuals, who lack interests in their own right, might be said to hold interests as an aggregate. With regard to wasps for instance, if an individual wasp is lacking morally considerable interests, the set of properties necessary and sufficient for its inclusion with the species *Vespula germanica* cannot rescue it from moral inconsiderability. Holists on the other hand, Rolston among them, conceive of species as something more than a class of individuals – rather, as entities or wholes in their own right with their own attendant interests.[23] Holists conceiving of species as interest-holding entities are thus able to attribute intrinsic value to them. Before a holist can move to make normative claims regarding the moral significance of species, they must first make strong ontological claims about our understanding of what a 'species' is.

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[20] For a helpful introduction to the ongoing debate between individualists see: Kristin Shrader-Frechette, 'Individualism, Holism and Environmental Ethics' (1996) Ethics and the Environment 1(1) 55.
[21] Carl Linneaus, *Systema Naturae 1735* (Nieuwkoop: Netherlands B de Graaf, 1964).
[22] For an accessible introduction to Classical Theory of Concepts, see: Eric Margolis and Stephen Laurence, 'Concepts' (Stanford Encyclopaedia of Philosophy, 2011) https://plato.stanford.edu/entries/concepts/ Last accessed 6th May 2019.
[23] Holmes Rolston III, *Philosophy gone wild: Essays in environmental ethics* (Amherst New York Prometheus (1986); Prometheus; Holmes Royston III, 'Value in nature and the nature of value', in R Attfield & A Belsey (eds.), *Philosophy and the Natural Environment* (Cambridge, Cambridge University Press 1994) 13.

Charles Foster perhaps hints at something similar when he claims that those seeking to uncover the special status of species should take as their starting point the 'high-kicking, impossibly co-ordinated chorus girls'.[24] At its most basic, Foster's claim is that the high levels of co-ordination between individuals partaking in some joint activity must indicate some or other special connection between individuals. Foster fleshes out this starting point by referring to other 'neurologically inexplicable' behaviours such as the flocking of birds and the 'shoaling' of fish.[25] With the exception of the chorus girls, the behaviour that Foster describes is more commonly understood as swarming behaviour.[26] Foster suggests that as the reaction speeds necessary for these creatures to move in apparent unison far outstrip those possible given the speed of neurological transmission, some other form of interconnectedness must exist. Foster appears to suggest that some or other form of Jungian Collective Unconscious is shared between all individuals of a species, enabling them to move as one. Because these individuals exist in a web of interconnectedness, Foster claims there exists some thing or other at the group or species level that is absent at the level of the individual.[27] Thus, according to Foster, the group is not only greater than the sum of its individual members, but it is also qualitatively different.

Such a claim does two important things. First, it places the ontological status of the species beyond reach of the class concept; on Foster's understanding, a species cannot be fully understood as a group of members belonging to a class. Importantly however, Foster's claims are not conclusive of ontological status given that in arguing that the web of interconnectedness instantiates some qualitatively different super-organism, we might doubt that Foster is arguing for a part-to-whole understanding of the ontology of species. For Foster, individual members of a species are not just members of a class, they are the constituent parts of a qualitatively different

[24] Charles Foster, *Human Dignity in Bioethics and Law* (Hart 2011) 14.
[25] Foster's claim actually relates to the 'schooling' of fish, not the rather different loose, uncoordinated shoaling of fish.
[26] For a helpful introduction to flocking and schooling behaviours see: David J T Sumpter, *Collective Animal Behaviour* (Princeton University Press 2010).
[27] Foster (n24).

whole. By way of analogy, Foster's part-to-whole conception applies as well to individual bricks building great palaces or individual blades of grass furnishing wide, open fields. As such, Foster appears to be arguing that the species is something substantively different in kind as compared to individual members of a species. Secondly, Foster identifies the existence of interests held by these species super-organisms and is therefore able to proceed to a full account of moral significance if he so wishes. Arguably then, Foster provides solutions of sorts to both the ontological question and the normative one.

However, there is good reason to consider Foster's status-conferring web of interconnectedness a dubious solution to the ontological question. In the first instance, Foster builds this idea of an interconnectedness on one central claim:

> When a flock of birds or a shoal of fish turns as one, or a line of chorus girls high-kicks in unison, the speed of reaction of the group is neurologically inexplicable in terms of the speed of reaction of the individual. The speed of transmission along the neurones of the individual is simply insufficient for the flock to wheel. But wheel it does. There is something mysterious and crucial happening at the level of the group that does not happen at the level of the individual.[28]

The central proposition here – that certain group acts or behaviours are neurologically inexplicable at the level of the individual – is drawn from Rupert Sheldrake's 'The New Science of Life'.[29] Sheldrake's 1981 work argues against conventional biological or physics-based understandings of the natural world, instead arguing for a basis in what he terms 'morphic resonance'. Sheldrake describes morphic resonance as the idea that systems within the natural world learn from previously existing similar systems. For Sheldrake, all species are enjoined in a shared collective memory stretching from the past into the present.

One need not look far to find volume upon volume critiquing Sheldrake's assertions regarding morphogenetics and parapsychology.[30] However, our concern here is the veracity of the claim to some neurological inexplicability of swarming behaviour. Sheldrake (and Foster) assume

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[28] Foster (n24) 13.
[29] Rupert Sheldrake, *A New Science of Life: The Hypothesis of Morphic Resonance* (J P Tarcher 1981).
[30] John Maddox, 'A Book for Burning?' (1981) Nature 245. Tim Adams, 'Rupert Sheldrake: The 'heretic' at odds with scientific dogma' (*The Guardian London* Sunday 5th February 2012) https://www.theguardian.com/science/2012/feb/05/rupert-sheldrake-interview-science-delusion Last accessed 27th December 2017.

that some neurological explanation is indeed necessary, and that in its absence the explanation must rely on ideas surrounding morphic resonance. In reality, many explanations aside from neurological ones exist to aid our understanding of swarming behaviours.[31] Given the weight and volume of scientific evidence contradicting Sheldrake's claims – claims upon which Foster builds his own arguments – there are good empirical reasons for doubting the soundness of Foster's foray into the species problem. However, in addressing these challenges Foster might avoid these empirical doubts by demanding a further level of abstraction. Whilst the co-ordinated whooping and whirling of starlings in the evening sky might not be indicative of any so-called 'cognitive hinterland' or shared collective memory, it is at least indicative of a high degree of cohesion among individuals. Foster therefore might find himself in good company, given that the some of the prominent arguments from philosophy of science base claims for the 'species as individuals' understanding on the cohesiveness of organisms belonging to that species.[32] In this way, Foster might solve the ontological question without recourse to Sheldrake. However, as Judith Crane has argued, 'cohesiveness' itself does not provide good cause for an ontological shift; such cohesion might also be adequately accommodated by the class conception of species mentioned above.[33] Thus, Foster fails to resolve the ontological question. However, Foster's is but one attempt to grant species a 'super-organism' like status.

Other attempts at ascribing moral significance to species on the basis that they are in fact their own entities have been more successful in resolving the ontological question. Larry Johnson, drawing on the earlier work of Hull, argues that a species can be recognised as a spatiotemporally localised individual.[34] According to Johnson, what ties a species together is not the existence of a shared property, but rather a genetic connection. Given that this genetic connection necessarily

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[24] David J T Sumpter, *Collective Animal Behaviour* (Princeton University Press 2010).

[32] David Hull, 'Are Species Really Individuals?' (1976) Systematic Zoology 174, 186–191.

[33] Judith Crane, 'On the Metaphysics of Species' (2004) Philosophy of Science 71(2) 156, 165; See also: Kitcher, 'Ghostly Whispers: Mayr, Ghiselin, and the 'Philosophers' on the Ontological Status of Species' (1987) Biology and Philosophy 2, 184–192.

[34] Lawrence Johnson, 'Humanity, Holism and Environmental Ethics' (1983) Environmental Values 345, 348; David Hull, 'A Matter of Individuality' (1978) Philosophy of Science 335, 340-341.

changes over time, it is not amenable to inclusion within a class concept as the properties both necessary and sufficient for inclusion within the class change continuously overtime. This overtly contradicts the classical understanding of natural kind or class concepts that expressly recognised the fixity of the relevant properties overtime. Therefore, on Johnson's understanding, species must be conceived of as individuals in their own right. Johnson's 'species-as-individuals' resolution of the ontological question finds the support of a good body of literature within theoretical biology and philosophy of science.[35]

The problem comes when Johnson includes a further consideration following his resolution of the ontological question. Once Johnson has, through his 'genetic connection' argument, established that a species is an individual, he stretches the parameters of the enquiry to ask whether species are 'entities'.[36] Already perhaps loading the die for his later explication of the normative question, Johnson resolves what he acknowledges to be a difficult issue, by offering Kenneth Sayre's definition of 'living system' as a place holder for the term 'entity'. Johnson does this with little explication or questioning – and certainly lacking any justification for treating as synonymous 'entity' and 'living system'.[37] However, having made the leap from species-as-individual to species-as-living-system, Johnson is now in a position to attribute interests to species. In describing species as living systems, he is able to note the ways in which they might be negatively or positively affected and ascribes interests accordingly. Such a move would not be possible if Johnson had concluded his ontological enquiry once the species-as-individuals thesis had been established. Rocks, blocks of cheese and cars can all be ascribed the ontological status of 'individual', however we would be hard pressed to recognise them as interest-holding living-entities or living systems. Therefore, it is this somewhat understated shift from individual, to entity, to living system, to living entity that

[35] For support of the 'Species as Individual' thesis from theoretical biology and philosophy of biology see: M T Ghiselin, 'A Radical Solution to the Species Problem' (1974) *Systematic Zoology* 23 536; David L Hull, 'Are Species Really Individuals?' (1976) Systematic Zoology 174.
[36] Johnson (n34) 349.
[37] Kenneth Sayre, *Cybernetics and the Philosophy of Mind* (New York 1976) 71.

does much of the normative groundwork, before the normative question has even be posed.[38] It is the elevation of species to a living entity that operates as the springboard for Johnson's arguments for interest-holding and, consequently, moral significance.

There are a good number of reasons to be sceptical of Johnson's argument. First, it is not clear why he should be so concerned to convince the reader that species, which he has already successfully argued should be recognised as individuals, should further be considered 'entities'. A plain language interpretation of entity would render the conclusion that it can be used interchangeably with individual. Both terms speak to the property of existing as discrete things.[39] Thus, the need to reason explicitly toward a further understanding of species as an 'entity' appears superfluous. What Johnson is instead focusing on is 'species as *living* entity' which, for the reasons suggested above, distinguishes it from inert individuals such as rocks and blocks of cheese and therefore yields certain normative pay offs.

The second problem with Johnson's claim lies in the suitability of Kenneth Sayre's definition of 'living system' for describing the ontological properties of the species-as-individuals thesis. It is not clear how species meet the requirements of 'low entropy' or 'equilibrium', crucial to Sayre's definition in anything more than an allegorical fashion.[40] Further, subsequent and arguably better received definitions of 'living system' fail to accommodate Johnson's claims entirely. James Grier Miller's seminal contribution to living systems theory recognises eight categories of living system; the cell, the organ, the organism, the group, the organisation, the community, the society and the supranational system.[41] Unsurprisingly, none of these eight categories are able to accommodate

[38] Note that Sandler & Crane draw up a similar criticism of Johnson in response to a latter restatement of this reasoning applied specifically to the question of the moral considerability of future generations. For our purposes here we are interested in Johnson's narrower treatment of the issue, focusing only on the possibility of the moral considerability of species. See: Sandler & Crane, 'On the Moral Considerability of *Homo sapiens* and Other Species' (2006) Environmental Values 69; Lawrence E Johnson, 'Future Generations and Contemporary Ethics' (2003) Environmental Values 471.

[39] See OED Definitions – Entity - "Being, existence, as opposed to non-existence; the existence, as distinguished from the qualities or relations, of anything." Individual – "One in substance or essence; forming an indivisible entity; indivisible."

[40] Sayre (n37) 71.

[41] James Grier Miller, *Living Systems: The Basic Concepts* (New York McGraw-Hill 1978).

Johnson's species-as-individual and therefore, on the received understanding of 'living system' we are unable to accommodate Johnson's claim. Given the species-as-individual thesis, species would, for the ontological claim to hold, have to sit at the level of the cell, the organ or the organism. If Johnson is to maintain the ontological claim to species-as-individuals, he has to give up the claim to interest holding, because the species-as-individuals conception does not present an entity capable of interest-holding. Instead, the species-as-individual conception provides an inert individual. However, if Johnson wants to develop the normative claim as to species holding interests, he has to give up on the ontological claim because according to contemporary systems theory the living system that Johnson describes cannot be conceived of as an individual. Thus, Johnson has to give up either his claim that species can be considered ontological individuals or the claim that they are living systems.

Understanding that Johnson makes unjustified leaps toward the end of his resolution of the ontological question leaves his probing of the normative question somewhat problematic. His foray into the normative question is entirely dependent on his understanding of the species as a living system – the inadequacies of which have been plumbed above. Given these inadequacies, Johnson fails to develop an account of species as an interest-holding entity. As such, despite Johnson's strong and justifiable ontological claims as to 'species-as-individuals', he is unable to put them to use in such a way that might elucidate the moral significance of species, and therefore makes no more ground (in fact arguably less) than his individualist counterparts.

Given the problems we have identified with conferring moral significance upon *species*, there appears to be no *intrinsic* moral value that can be attached to the concept. Species cannot claim for themselves the right not to be eliminated, in part at least because there is no way of vesting them with the requisite interests on either an individualist or holist account. Whilst there are surely free-standing extrinsic concerns that exist with regard to eliminating species, these revolve around the purposes for which the drive is used. For instance, removing a species that supports other morally considerable individual beings might invoke certain extrinsic moral considerations. Such an

example might occur if we were to eliminate dormice, causing the local Barn Owl population to starve. In this context, the population suppression drive has caused harm or suffering to another morally significant individual. As such, any attempt to ground a moral prohibition for population suppression drives on concern for the species themselves likely fails. Below, I turn to consider whether a moral prohibition for either sort of drive (population replacement or population suppression) might be grounded in concern for human overreaching instead.

The discussion above has demonstrated that neither individualistic nor holist accounts are able to provide for the moral considerability of species as a concept. Any moral prohibitions on the elimination of species instead must rest on considerations that exist at the level of the individual, in other words, that elimination curtails the interests of some morally relevant entity. Where elimination is achieved by physical or chemical means – traps or poisons – the way in which these interests are curtailed is clear in the context of organisms with a capacity for suffering. In those cases, the moral prohibition flows from the suffering of individual members of the species. As has been suggested above, the difficulty that population suppression drives pose is that we cannot readily identify the curtailment of the interests of the individual.

In the context of gene drives then, and population suppression drives that operate by fixing the sex of the modified individual, it is difficult to articulate such a modification as a curtailment of the individuals interests or harm in a morally relevant way. As such, I conclude that there is no intrinsic moral prohibition on the use of gene drive technologies for the purposes of population suppression. Instead, the ethical quality of those gene drives is contingent on the properties or characteristics of the individuals of the particular species being manipulated, or the ecological consequences of the eradication of that species. Pursuing an enquiry into the ethical qualities of any given application of gene drive technologies, and drilling down into its ethical particularities, places on screen a range of overflows and target agents that are otherwise overlooked by technical expertise. The necessary analysis broadens our understanding of the technologies, and whilst some of the considerations it raises require technical expertise in order to answer, those crucial questions

would be left unarticulated by a focus on technical expertise alone. The discussion below points to one instance in which the characteristics of the candidate species, not taken account of by technical understandings, will render the use of gene drive technologies for species eradication impermissible and therefore ought to be an important part of the frames that we build.

1.3 Relational Accounts of Value - A Third Way?

Relational accounts of personhood contend that it is not individual capacities, capabilities or interests that ground moral status, but rather certain sorts of relationships that exist between beings. In that way, relational accounts of personhood might provide a means of conferring moral status on species as a concept, in the absence of interests held by individual members of those species.

Herring and Foster contend it is relationships of care that generate moral value, whilst others discussed below argue that the hallmark of moral value is the capacity for relationships of a certain kind.[42] In taking as morally considerable relationships rather than individuals, relationalists escape the follies of capacity-based individualist accounts that exclude infants and the mentally disabled from moral consideration. However, it is often suggested the relationalists themselves are committed to counterintuitive positions – for instance, in denying moral status to adult humans bereft of any caring relationships (the so-called "Robinson Crusoe problem").[43] For our purposes, we will consider the relational account of moral status offered by Thaddeus Metz. Metz is a relational theorist seeking to overcome the pitfalls of individualism and holism as we encountered them in the discussion above.[44]

In this section I explore the ways in which a relational account might be able to aid or advance our explorations of the moral permissibility of population suppression drives. This analysis notes a range of overflows that, on other enquiries, go overlooked. We noted above that

[42] Charles Foster and Jonathan Herring, *Personhood, Identity and the Law* (Springer 2017) 38.
[43] Ibid.
[44] Thaddeus Metz, 'An African Theory of Moral Status: A Relational Alternative to Individualism and Holism' in M Chemhuru (ed*) African Environmental Ethics* (Dordrecht Springer 2019).

neither individualist nor holist accounts are able to articulate or identify any harm to interests, as committed by population suppression drives and so take this issue as our point of critical departure. What follows demonstrates the ways in which this particular ethical enquiry provides a range of questions that need to be answered if at least some epistemic uncertainty is to be overcome. Furthermore, for the most part the questions articulated are answerable only by technical expertise. In this way, we can observe the role that ethics might play in developing and structuring our technical understandings of new technologies and their implications.

1.3.1 Thaddeus Metz's Relational Account of Moral Status

Thaddeus Metz describes his relational account of moral status as standing between individualist accounts and holist accounts.[45] Like individualists, Metz attributes moral status on grounds other than group membership and like holism, Metz argues that his relational account does not accord moral status on the basis of intrinsic properties alone. According to Metz the key to identifying whether an organism (or, presumably, group) has moral status is asking whether that entity has the *capacity* to engage in a communal relationship of a certain kind.

1.3.1.1 Applying Metz Account to Gene Drive

By his own lights, Metz's account would do little to intervene in discussions regarding the moral permissibility of population suppression drives. This is because when thinking about the communal relationships we admit of as morally relevant, the human is sovereign. Metz's relational approach considers the relationships that exist between humans and other entities rather than relationships as they exist either between two or more non-human entities of the same kind, or two (or more) different kinds of non-human entity.

Metz makes this admission when he discusses how his theory would handle the moral status of a complex alien species capable of demonstrating the communal relationships he requires

[45] Ibid.

amongst its own kind, but unable to share in such relationships with humans when they reach *terra firma*. He says:

> …If I had to choose between rescuing a member of another species that were capable of friendly relationships with us and one that were not, I would judge myself to have more moral reason to save the former, which might be best explained by its having a greater moral status. [46]

In the absence of the hypothetical absolutist trade-off (rescuing one entity or the other) that he proposes there is still room to attribute at least some degree of moral status to the Martian. The relational account does not leave the Martians bereft of moral status altogether, rather it attributes a degree of moral status insufficient to overtop the interests of the other being also in need of rescue. In this way, then, in the context of highly socially complex entities at least, Metz's relational account is able to operate without human dominion of the "communal relationships" that we have moral reasons to care about. Further, given that what other theorists require for the instantiation of personhood is a "relationship marked by care", we might think that this criterion can be satisfied in the absence of humans, either as carer, or cared for.[47] For our purposes then, we can understand the communal relationships necessary for the instantiation of moral status as those relationships marked by care (or the capacity to care), not necessarily involving humans.

As it happens, relationships marked by care as described by Foster and Herring appear to share not insignificant ground with those relationships of solidarity and reciprocity that Metz requires.[48] Given that we have established the possibility of a relational account attributing moral status to non-human relationships and non-human individuals, we might find instructive test cases closer to home than Metz's Martians. I suggest that there are at least two candidates that might benefit from consideration by relational accounts; species demonstrating eusocial behaviours and mammal species with a high degree of both sexual dimorphism and sociality – each category will be considered in turn below.

a) Eusocial Species

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[46] Metz (n44) 395.
[47] Such a notion is clearly entertained by Foster and Herring, with reference to the work of C Safina. See: C Safina, *Beyond words: what animals think and feel* (Henry Holt, New York 2015).
[48] Foster and Herring (n42) 27.

Eusociality as understood by behavioural ecologists is the highest recognised form of social behaviour. Eusocial species are those demonstrating co-operation in caring for young in colonies where there is only one reproducing female.[49] Oftentimes, colonies have castes of workers with defined responsibilities either caring for young, providing food, or maintaining the colony's habitat. Ants, wasps and bees are among the invertebrates we recognise as Eusocial, with certain sub-species of mole rat being the only eusocial mammals.

Eusocial invertebrates are perhaps the most interesting for our purposes for two reasons. The first, a pragmatic one: ants, wasps and other such creepy crawly pests are likely candidates for gene drive technologies in the not too distant future. Secondly, these eusocial invertebrates do not possess any of the intrinsic properties that might provide for a moral prohibition of gene drive on an individualistic account. That is, they bear no capacity for suffering (amongst other relevant properties). As such, it might be these sorts of species for whom a relational account might be able to do the most legwork, if successful.

b) Do Eusocial species demonstrate the relevant "communal relationships"?

In the last section, contrary to Metz, we charted the possibility that a relational account might attribute moral status to entities partaking in communal relationships which did not involve human beings. I have suggested that the possibility exists for communal relationships of the morally relevant kind as between entities of the same kind, and two or more entities of different kinds. That is, for example, communal relationships of the morally relevant kind between two ants on the one hand or between a human and a dog on the other. Thus, in the Martian example, we might be able to say that because of the communal relationships the Martians share with each other, relational accounts are capable of attributing at least some degree of moral status to Martians. The question in this section then is whether the communal relationships demonstrated by Eusocial species are of a morally relevant kind. In engaging in this analysis below, I argue that we hit upon

[49] Edward O Wilson and Bert Holldobler, 'Eusociality: Origin and Consequences' (2005) Proceedings of the National Academy of Science 13367.

a further flaw in Metz's account. This is the idea that what stands behind Metz's "capacity for communal relationships" is a presupposition for a number of intrinsic properties and, as such, Metz's theory is, in fact, far more individualistic than he might, in plain text, admit.

Metz defines the morally relevant communal relationships as those "in which people identify with each other and exhibit solidarity with one and other". This definition, taken in connection with the elucidation of how his theory operates, suggests that there exist some significant cognitive preconditions for the communal relationships and the capacity necessary to partake in them that Metz requires. For example, Metz argues that early term foetuses are excluded from moral calculus given that they bear no capacity for the types of communal relationships that he requires.[50] We might assume he reaches this conclusion because they are absent any indications of the traits that make a capacity for such things as solidarity and self-and/or other identification possible. On the other hand, Metz maintains that infanticide is wrong, by means of attributing to new-borns the capacities he requires.[51] As such, it would seem that as a minimum, Metz's account requires some capacity for self-awareness, amongst other arguably complex cognitive traits. That being the case, the sorts of communal relationships demonstrated by eusocial creatures likely fall short of the mark for Metz. They are instead, he might argue, brute facts of evolutionary biology, rather than evidence of a shared and reciprocal pursuit of flourishing. In this way, then, Metz's account appears more reliant on the existence of intrinsic properties than he admits and, arguably, offers no more moral intervention for eusocial invertebrate species threatened with a population suppression drive than individualist accounts can, despite high levels of sociality and relationality. The objection to Metz's theory that I make here is not that in failing to bring eusocial invertebrates into the realm of moral considerability Metz has erred but rather that Metz's account specifically and relational accounts generally are not necessarily as expansive (or indeed non-individualistic) as theorists claim them to be.

[50] Metz (n44) 399.
[51] Ibid 400.

c) Do some sexually dimorphic, socially complex species demonstrate the necessary "communal relationships"?

Sexually dimorphic species are those with well-defined, highly differentiated characteristics between the sexes that extend beyond their sexual organs. Oftentimes these characteristics relate to size, markings or colours, but some species exhibit behavioural dimorphism too. Behavioural sexual dimorphism is demonstrated by highly differentiated sex roles in child rearing and resource gathering. Sexual dimorphism is a highly relevant, though little understood aspect of pathogen transmission in a range of vector species and mosquitos in particular.[52] As such, many of the current candidate species demonstrate the sexual dimorphism described here.

Elephants are highly social animals, with strong matriarchal social structures and pronounced sexual dimorphism. Whilst the male of the species live solitary existences from puberty, females live in herds of closely related individuals, sharing the burdens of child rearing and resource management. The role of dominant females within elephant social groupings has been shown to be vital to the physical and psychological health of elephants both wild and captive.[53] Elephants are a good example of a highly socially complex species with marked sexual dimorphism but others include lions, gibbons and manatees.[54] Further, as relational theorists have noted elsewhere, elephants are a non-human species capable of the relationships of care required for the instantiation of moral status.[55] These relationships of care are however, vulnerable to harm or curtailment by the use of population suppression drives. Given the role of female individuals within the species social structure, it is not difficult to recognise the importance of stable sex ratios over time. Either an increase or decrease in the number of females born to a herd over time

[52] Molly Duman-Scheel and Zainulabeuddin Syed, 'Developmental neurogenetics of Sexual Diamorphism in *Aedes aegypti'* (2015) Frontiers in Ecology and Evolution 61.
[53] R Sukumar, 'The Management of Large Mammals in Relation to Male Strategies and Conflict with People' (1991) Biological Conservation 93,
[54] For a useful introduction to the implications and relevance of sexual dimorphism for social behaviour and organisation see: Clutton-Brock, Guiness and Albon, *Red Deer: Behaviour and Ecology of Two Sexes* (University of Chicago Press, Chicago 1982).
[55] Herring and Foster (n42) 38. See also: C Safina, *Beyond Words: What Animals Think and Feel* (Henry Holy, New York 2015).

destabilises the community's social structure, resulting in both physical and psychological harm to individuals within the herd. A scarcity of females might lead to group aggression or the starvation of the herd's less mature members.[56] On the other hand, an overabundance of males within elephant populations can lead to resource scarcity, which in turn increases crop raiding behaviours adversely affecting human neighbours.[57] These increased crop raiding behaviours cause conflict between elephants and humans, oftentimes leading to physical harm for both groups. Thus, altering sex-ratios (as population suppression drives would be bound to do) creates the risk of significant harm, both to members of the herd and the humans with whom they share their environment. In these ways, we can see that the population suppression drive is capable of harming the morally worthwhile relationships that exist between elephants, and as a consequence also harming individual members of the species and those with whom the individual shares their habitat.

Individualist accounts of moral status are unable to capture the values that exists in these relationships or express these valuable relationships as interests in need of moral consideration. Individualist accounts merely ask whether the individual in question has moral status, and, if the answer is yes, whether the proposed course of action harms the interests that we have reason to consider. This enquiry can be divided up into two-parts – the Status question (i.e. Is the entity in question morally considerable?) and the Interest Question (i.e. In doing what is proposed are the entity's interests curtailed?). As such, in the context of population suppression drives for elephants, the individualist would ask:

> Does the elephant have moral status?
>
> > Yes – because it possesses the capacity for suffering.
>
> Does the population suppression drive curtail the interests of the individual modified?

[56] R Sukumar, The Living Elephants: Evolutionary Ecology, Behaviour and Conservation (Oxford University Press 2003) 136.
[57] R Sukumar & M Gadgil, 'Male-female differences in foraging on crops by Asian elephants' (1988) Animal Behaviour 1233.

No.

Therefore, the gene drive designed to suppress elephant populations by distorting sex ratios would be morally permissible. In contrast, the relational account would ask:

Does the elephant have moral status?

Yes – because it demonstrates relationships marked by care.

Does the population suppression drive curtail those relationships?

Yes.

Therefore, the relational account gives us pause by way of cashing these relationships out as morally valuable interests requiring consideration and perhaps even protection. There are, however, obvious criticisms of this approach. Metz himself would eschew the phrasing of the interests question, given that it focuses on actual relationships, rather than the capacities for those relationships. That being the case, the Robinson Crusoe problem re-emerges – how can an intuitive and rational theory of moral status exclude from its ambit those otherwise morally considerable beings that exist in a social vacuum? Of course, if in acknowledging this dilemma we choose to revert to Metz's capacity-based account we find our response to the "interests" question to be the same as that rendered by a straightforward individualistic account. In this way, Metz moves a lesser distance from the individualist account he chides than he might realise.

Given these problems, my hopes for the use of a relational account in assessing the moral permissibility of gene drive technologies are somewhat more modest than accounting for the moral considerability of species either as a concept, or any given species in particular. Rather, my aspirations for the use of a relational account are more pragmatic insofar as I advocate for the application of such an account in seeking to expose novel but morally relevant harms that would not otherwise be recognised by either individualist or holist accounts. In other words, I hope to have shone some light on the ways in which ethical enquiries might aid the framing process, by

revealing otherwise overlooked overflows. Instead of looking to relational accounts for the instantiation of moral status, we should look to them in order to broaden the range of interests we conceive of as morally considerable, and those that regulation ought to take account of. We return to the practicalities of applying such an approach in the regulatory context at the end of this Chapter.

2. The Ethics of Population Alteration

The foregoing analysis scoped the ethical concerns associated with population suppression drives, in particular, the moral considerability of species as a concept. This section focuses on the ethical issues as they relate to population alteration drives. As such, the question here is whether there can be any sustainable ethical qualms about altering the gene pool at the population level. Some have conceived of population alteration drives as attempts to 'sculpt evolution'.[58] Certainly, gene drive technologies, given their super-mendelian nature, are an attempt to direct or intervene with the path that evolution would otherwise follow. However, unlike population suppression drives, these population alteration drives can have very real consequences for individuals too – many of them reflecting concerns that we might have in the context of more mainstream genetic modification.

The enquiry necessarily proceeds with two questions in mind. Firstly, are the changes to the individual organism that population alteration drives introduce problematic? And, secondly, is the population level change brought about by alteration drives problematic in and of itself or, in other words, is it ethical to sculpt evolution? Along the way, a number of concerns emerge, that are not revealed or understood through technical understandings alone. Instead, we identify a number of overflows that are otherwise overlooked, and yet vital to the ways in which we ought to understand gene drive technologies if we are to construct frames that bear fidelity to the phenomena that we are trying to regulate.

[58] Kevin Esvelt, 'Engineering Biology in light of Evolution' (*Sculpting Evolution,* 2019) http://www.sculptingevolution.org Last accessed Sunday 14th April 2018.

2.1 Problematizing the Issue

At first blush, given that gene drive technologies alter the course of a species' evolution, one might be tempted to advance a comparison between population alteration drives and the human enhancement debate. Michael Sandel's objection from humility and his concern for its degradation might appear to be as pertinent here as in the human context.[59] Our desire to alter entire species for our own ends appears to be as good a demonstration of our departure from acceptance of 'the natural' as any. However, there is good reason to be sceptical of attempts to problematize the issue this way. For instance, it is not clear that in all cases the modification that a gene drive confers can rightly be considered 'enhancement'. In some instances, the change that the gene drive propagates has no discernible effect on the target organism for its own sakes. When the Hammond *et al* drive makes mosquitoes insusceptible to infection by the *Plasmodium* parasite, this newly conferred insusceptibility provides neither benefit nor burden to the mosquito itself, rather only a benefit for the human populations with which it shares an environment. Whilst a much-vexed debate seeks to distinguish (if indeed, such a distinction can be made) between modifications that constitute 'treatments' and modifications that constitute 'enhancements' in the human context, the notion of enhancement has little to no purchase on the question in hand.[60]

In truth, Sandel might respond by arguing that whether the change that a gene drive introduces constitutes an 'enhancement' need not be established. The lack of humility that so troubles Sandel in the context of enhancement is equally demonstrated by our willingness to interfere with the genomes of other species, regardless of the subjective value we attribute to those interferences. Put simply, acting on the desire to effect population level changes in other species is quite enough to constitute a troublesome assault on our humility.

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[59] Michael Sandel, *The Case Against Perfection* (Harvard University Press 2009).
[60] Frances Kamm, 'Is there a Problem with Enhancement?' (2005) The American Journal of Bioethics 5(3) 5. For a statement of the opposing view see: P H Schwartz, "Defending the Distinction between Treatment and Enhancement' (2005) The American Journal of Bioethics 5(3) 17.

However, Sandel's argument fails to provide for the moral impermissibility of gene drives in other, important ways. Aside from humility, Sandel is equally concerned with the social practices of solidarity and responsibility – practices that for him define key features of our moral landscape.[61] These relational aspects of the arguments that Sandel and his supporters are given to make find themselves somewhat attenuated once we step beyond the context of modifications of humans, by humans. Gene drives are, instead, modifications of non-humans, by humans. Given the quite different relationships, one might ask how the modification of other species threatens the very human social practices of solidarity, responsibility and humility. These are virtues and social practices that exist between the modifier and the modified and which can be participated in and pursued by both. Enhancement disrupts or changes the nature of the relationships between the modifier and the modified in a bi-lateral manner, altering the way both participate in and engage with the social practices of solidarity and responsibility. By contrast, in the gene drive context, the target organisms – modified or not – do not and cannot participate in these goods. There is no social practice of solidarity or responsibility between and amongst humans and the target organism to be denigrated or destroyed.

That is not to say that there are no duties of stewardship owed by humans in relation to the natural world about them, undoubtedly there are, but rather that such duties do not constitute a social practice of the kind that Sandel values.

Whilst there is no apparent social practice of solidarity or responsibility to be undermined, the question of whether modifying other species degrades our own humility remains open. If we are given to accept that modifying ourselves and our children offends the virtue of humility in myriad ways, perhaps we can also argue that the desire for mastery over other species does too? However, the suggestion that certain expressions of mastery might degrade our humility is an empirical claim. Humans have exercised mastery over other species and directed evolution for

[61] Sandel (n59) 86.

centuries – we have textual evidence of selective breeding of cattle and wheat from the dawn of the Carthaginian Empire.[62] If we are concerned that the development and deployment of gene drive technologies might degrade our humility, we should perhaps first ask whether the use of selective breeding and species domestication has led to similar consequences. Section Two will discuss selective breeding rather than genetic enhancement as the baseline ethical comparator for gene drive technologies. Only in understanding whether selective breeding raises a troublesome challenge to our humility might we begin to understand whether the mastery that gene drive entails does so too.

Ultimately, whether we consider the use of gene drive technologies to be an impermissible demonstration of hubris or human overreaching is likely to be determined by reference to the purpose the drive seeks to fulfil. When Edward Jenner developed a vaccine that would eventually lead to the worldwide eradication of the smallpox virus, suggestions that such a technological advance demonstrated an impermissible pursuit of mastery would and should not have been countenanced.[63] The suggestion that the death and suffering caused by the small pox virus ought to be tolerated due to an ethical need to conserve the virus could not be justified on consequentialist, deontological or dignitarian grounds.[64] Similarly, no one would object to the current and ongoing efforts to eliminate the polio virus for the same reasons. Thus, it seems to be the case that concerns regarding mastery are taken account of in the context of that technology's particular purpose. Gene drive technologies deployed for trivial purposes might well run aground the mastery objection even where they cause no tangible harm. For example, a gene drive that sought to change the stag beetle population from dull black to the aesthetically preferable yellow might cause no physical harm to the stag beetles themselves, and yet we might still find it an impermissible feat of human overreaching. However, those gene drives that entail a significant

[62] Richard Miles, Carthage Must Be Destroyed: The Rise and Fall of An Ancient Civilization (Penguin 2010).
[63] Harry Bloch, 'Edward Jenner (1749-1823): The History and Effects of Small Pox, Inoculation and Vaccination' (1993) JAMA Pediatrics 772.
[64] Arthur J Caplan, 'Is Disease Eradication Ethical?' (2009) The Lancet 2192.

public health benefit would likely be considered permissible nonetheless because, oftentimes, the line between laudable human advancement and human overreaching is difficult to trace. Whether judging the permissibility of an apparent pursuit of mastery by reference to the benefits it can yield for human populations is, in itself, problematically determined by a logic of utilitarian anthropocentrism, remains an open question.[65]

Concerns regarding human overreaching that the likes of Sandel raise might well be those most difficult to shake for the more cautious proponents of gene drive technology. Inevitably, these questions are bound to other complex issues such as the legitimacy of the scientific imperative,[66] the value of knowledge for knowledge's sake and, further, incentive structures within research and development.

With regard to the scientific imperative, in the gene drive context it is clear that is not a desire to realise the eradication of vector-borne diseases alone that drives progress. Since Hammond *et al's* proof of principle was first published in 2015, laboratories and research groups who began by developing drives for the purposes of controlling and eradicating vector-borne disease have already moved to programmes of research developing gene drives in mammalian species without an articulated public health purpose or benefit.[67] We might assume, then, that gene drive's onward march in the research setting will be orientated less and less by the eradication of vector-borne disease, as technological capabilities expand the range of possibilities beyond insect applications. The door to the use of gene drive technologies with less laudable, or more trivial purposes is already open. This concern is exacerbated further given the oftentimes serendipitous nature of scientific advancement, scientists are often unable, or unwilling, to articulate the purpose

[65] Bernard Williams, 'The Human Prejudice' in Bernard Williams (ed) *Philosophy as a Humanistic Discipline* (Princeton University Press 2006).
[66] Dan Callahan, *What Price Better Health? The Hazards of the Research Imperative* (University of California Press 2006). See also: Rebecca Dresser, 'Alive and Well: The Research Imperative' (2012) The Journal of Law, Medicine & Ethics 915.
[67] Grunwald, Gantz. Poplawski, Xu, Bier & Cooper, 'Super-Mendelian Inheritance Mediated by CRISPR/Cas9 in the Female Mouse Germline' (2019) bioRxiv < https://www.biorxiv.org/content/10.1101/362558v2> Last accessed 20th February 2019.

of their enquiry at the stage of basic research.[68] Others likely regard the notion that science can be advanced by articulating a desired outcome and driving linearly toward it to be one bound up in a misunderstanding of the scientific method.[69] This is in itself the manifestation of a problem that dogs the wider arena of science and policy making. For now, it is important to note whether it may be practical to require scientists to articulate the overarching aim or purpose of their research in order to ascertain whether such research constitutes a demonstration of hubris or overreaching. We will consider how some of the insights raised here might factor into regulatory decision making later in this Chapter.

2.2 Analogy with Selective Breeding

Selective breeding, rather than genetic enhancement, is a more desirable starting point for exploring any ethical uncertainties that might exist with regard to gene drives for population alteration. The genetic modification of individuals does not raise evolution-based concerns in the way that selective breeding does. Unlike selective breeding, the genetic modification of animals seldom leads to intergenerational genome changes and therefore population alteration. This is for a few reasons. Often, the genetic modifications that we introduce confer fitness disadvantages that see them selected against. Secondly, and more practically, we rarely breed from those animals that we do modify – most usually because they are commercial food stock, and thus slaughtered prior to sexual maturity. Given the relevant similarities to gene drive, selective breeding rather than genetic enhancement or modification ought to be our preferred ethical baseline.

Along the lines of arguments made elsewhere in the ethical literature, this section assumes that selective breeding is ethically unproblematic.[70] However, several significant objections to this

[68] For instance, Alexander Flemming's discovery of penicillin on the festering agar plate and the development of Viagra from drugs intended for heart pain are just some of the more well-known example of the serendipitous nature of medical research. For a rather enjoyable discussion of the phenomena see: Morton A Meyers, *Happy Accidents: Serendipity in Major Medical Breakthroughs in the Twentieth Century* (New York Arcade Publishing 2007).

[69] There has been much discussion of the tensions between the scientific method and regulation with regard to debates surrounding the regulation of research on human embryos, and particularly in debates surrounding a proposed extension of the 14-day rule. See: Nuffield Council on Bioethics, 'Time Limits on Maintaining Human Embryos in Research (London: Nuffield Foundation, 2016).

[70] Julian Savulescu "Genetic Interventions and The Ethics of Enhancement of Human Beings", in Bonnie Steinbock (Ed), *The Oxford Handbook of Bioethics* (Oxford University Press 2007).

position exist. These include the instrumentalization of animals, welfare-based concerns and concerns about the reduction of intra-species genetic diversity. Two of these three concerns – instrumentalization and welfare – are also present in debates concerning the ethics of more traditional genetic modification techniques. Once the ethical concerns regarding selective breeding have been explored and dismissed, we will turn to consider whether gene drive technologies present any points of dis-analogy so prominent as to instantiate sustainable ethical concerns.

2.2.1 Objection from Instrumentalization

This objection suggests that altering an organism for the benefit of human ends might be morally impermissible for failing to attend to the ends of the organism itself. It is important to note that these sorts of arguments are active at the individual rather than species level and are as relevant to genetic modification as selective breeding. What objectors are concerned with here is the effect that selective breeding has on individual organisms, not the population as a whole. For this reason, these arguments or objections are more tied to conventional understandings of harm to the interests of individuals. Although to be clear, we can presumably think of problematic instances of instrumentalization that do not cause harm where harm is understood as the infliction of pain or the curtailment of interests. Just as any Kantian would object to the instrumentalization of one person by another, so too should we be concerned by the instrumentalization of non-human organisms by humans, or so the argument goes. As such, selecting for cattle without horns for the purposes of reducing the possibility of harm to humans, other livestock and agricultural machinery and not for the cattle's own sake, fails to demonstrate the sort of respect the animal is owed. Many have characterized this lack of respect as an affront to the animal's 'dignity'.

In 2001, the Swiss Federal Ethics Committee described a number of animal dignity violating acts including the alteration of appearance and undue instrumentalization.[71] 'Dignity talk' has gained traction in academic circles too, despite calls to replace the notion, said to be void of

[71] The Dignity of Animals, 'A Joint Statement by the Federal Ethics Committee on Human Biotechnology (ECNH) and the Federal Committee on Animal Experiments' (FCAE) (2001)

descriptive power, with 'integrity' instead.[72] For the most part, these sorts of arguments fail to establish any 'intrinsic moral concerns' with regard to selective breeding.[73] Instead, the moral concerns are identified are 'extrinsic', resting on issues of animal welfare or risk. As Alasdair Cochrane notes, the Kantian prohibition on using others as ends is not *absolute*.[74] Cochrane suggests that the prohibition only excludes using things *solely* as a means – insofar as the instrumentalization does not extinguish all opportunities for well-being, there has been no moral violation. Therefore, even if we accept that the Kantian position can be extended to animals, it would seem that concerns regarding instrumentalization can be distilled down into concerns for welfare.[75] As such, whether an application of gene drive technologies is or is not problematic from the perspective of instrumentalization will depend upon whether the trait selected for causes any welfare interference.[76]

2.2.2 Objection from Animal Welfare

Following the publication of Peter Singer's *Animal Liberation* in 1975, a growing corpus of literature has claimed moral equivalence between animals and humans. Taking Singer's welfarist claims as their foil, Tom Regan and Gary Francione have developed even more ambitious rights-based claims for animals.[77] However, these positions remain outside the philosophical mainstream.[78] For our purposes here, we will consider the somewhat weaker claim, that because we must give an

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[72] Michael Hauskeller, *Biotechnology and the Integrity of Life: Taking Public Fears Seriously* (Routledge 2007) 18-28.
[73] MJ Reiss, and R Straughan, *Improving Nature: The Science and Ethics of Genetic Engineering* (Cambridge University Press 1996)
[74] Alasdair Cochrane, *Animal Rights Without Liberation: Applied Ethics and Human Obligations* (Columbia University Press 2012) 107-109.
[75] Not all agree on this matter, as the Kantian formulation has in mind *persons* – a status that cannot be extended to non-humans. For a compelling account extending Kantian protection to non-humans, see: Christine M Korsgaard, *Fellow Creatures: Our Obligations to the Other Animals* (Oxford University Press 2018).
[76] I pause here to note that concerns for instrumentalization and dignity are not unilateral – we can, and should, hold concern for the dignity of both the modified and the modifier. In this respect, there are likely sustainable objections to instrumentalising an individual organism on account of instrumentalization presenting an afront to the dignity of the instrumentaliser. I do not dispute this claim, rather I support it. However, I consider that such concerns are adequately accommodated by Michael Sandel's objection from humility as explicated above. Any instrumentalization sufficient to constitute an afront to the instrumentalisers dignity, must also be sufficiently humility degrading as to also elicit objections from Sandelians.
[77] Tom Regan, *The Case for Animal Rights* (University of California Press, 3rd Ed 2004); Gary L Francione, *Rain Without Thunder: The Ideology of the Animals Rights Movement* (Temple University Press 1995).
[78] As Cochrane notes, see Cochrane (n36) 3.

affirmative answer to the Benthamite enquiry (can they suffer?) animals have interests which should not (without good reason) be thwarted.[79] On this view, then, selective breeding is only morally impermissible when it causes harm.[80] To be sure, there are indeed widespread examples of selective breeding causing harm. Few are unaware of what have now been coined 'genetic welfare' issues – for example, selectively breeding for dogs with short noses who, as a result, suffer the respiratory problems we see in pugs and bulldogs.[81] In these cases, we can quite plainly understand the harm and the attendant moral prohibition. There are, however, more difficult cases and at this point it is helpful to note that the gene drive context is littered with more difficult cases than easy ones. Focusing on selective breeding however, we see hard cases in the context of animals such as the 'Parlor Roll' Pigeon, a domesticated bird bred to be flightless and to adopt instead tumbling or rolling as its primary mode of travel. In this instance it is unclear whether the bird's lack of flight causes it harm – it might well be the case that despite its inability to do the things pigeons usually do, it finds great pleasure in tumbling about its environment. In these cases, welfare issues cannot be easily ruled in or out of the frames that we build. Thus, objectors to this sort of selective breeding might instead rely on some of the dignity-based issues noted briefly above. In any case, these objections to selective breeding are only contingent on the genetic modification wrought. It is by virtue of effecting *certain sorts* of changes, rather than effecting changes *per se*, that selective breeding becomes morally problematic. In the context of gene drive technologies then, whether concerns regarding the welfare of the edited organism ought to form part of our framing for understanding the technology will depend on the effects of the genetic modification selected, insofar as those effects can be known.

[79] Bentham (n2). This individualistic, interest-based position has been propounded by various scholars. For instance see: Joel Feinberg, 'The Rights of Animals and Unborn Generations' in W T Blackstone (Ed) *Philosophy and Environmental Crisis* (University of Georgia Press 1974); Bernard E Rollin, Animal Rights and Human Morality (New York, 3rd Ed 2006) 115; James Rachels, *Created From Animals: The Moral Implications of Darwinism* (Oxford University Press 1990) 207.

[80] This discussion is not so different from the discussion of moral significance in I above.

[81] James Kirkwood, 'Selective Breeding: Making the Welfare Consequences Clear' (2012) Veterinary Record 535, 536.

2.2.3 Objection from Evolution

This objection encapsulates what might be the core of the issue explored here – is it *prima facie* wrong to effect population level genetic changes that would not otherwise occur through natural selection? That is to say, is it wrong to effect changes that would not be brought about by evolution, thus changing the path of evolution for that species? Here, we do not need to focus on the consequences of those changes such as the welfare-based concerns discussed above. Instead we are asking whether the mere fact of intervening in evolution through selective breeding is in and of itself ethically problematic. This issue is somewhat fraught within the literature. The likes of Julian Savelescu find directing evolution ethically unproblematic, but are not explicit in their reasoning.[82] Others, drawing on arguments against the unnatural, discussed further below, raise objections which are not on their face ethical in nature.[83] Further, recalling the Sandelian arguments explored above, it might be argued that sculpting evolution does indeed lead to an impermissible assault on our own humility.

2.3 Gene Drive Dis-Analogy?

So far it has been established that there exist no intrinsic moral objections to selective breeding. Those objections that do exist are extrinsic, relating to the purpose for which selective breeding is used, or the consequences it has for individual organisms. Having established selective breeding as our morally acceptable baseline, we now move to ask whether gene drive as a technology is sufficiently different to instantiate sustainable moral objections. As such, this section points to two relevant differences between selective breeding and gene drive: rapidity, and 'unnaturalness'. Concerns about rapidity focus on the notion that gene drive is able to effect total population level changes in far fewer generations than traditional selective breeding techniques, due to the supra-mendelian biasing of inheritance. Selective breeding relies on mendelian rules of inheritance, and

[82] Julian Savelescu, 'New Breeds of Humans: The Moral Obligation to Enhance' (2005) Reproductive Biomedicine Online 36.
[83] Nuffield Council of Bioethics, '(un)natural: Ideas about naturalness in public and political debates about science, technology and medicine' (London: Nuffield Foundation, 2015).

so bringing about total population changes might well take hundreds of generations and, depending on the life span of the species, decades or even centuries. In stark contrast, in species such as mosquitoes with short life spans and short intergenerational periods, total population alteration might be brought about in weeks and months.

Concerns about the unnaturalness of gene drive might also encapsulate concerns about rapidity, however, the specific understanding of 'unnatural' as adopted here denotes concerns regarding the introduction of foreign phenotypes. That is, whilst selective breeding is thought to only promote the prevalence of a pre-existing phenotype contrary to evolution, gene drive can introduce phenotypes that are not otherwise found within that species. Selective breeding exaggerates a trait that was already there (in a way that would not ordinarily be selected for by evolution), whereas gene drive technologies can cause the biased inheritance of entirely new traits. For example, whilst most cattle have black coats, a selective breeding program might produce whole herds of red coated cattle by ensuring the presence of the recessive red coats alleles in mating pairs. Conversely, with gene drive, we might introduce genetic information from an entirely difference species, to effect genetic changes that code for parasite resistance.

Of the two sites of dis-analogy identified, rapidity is perhaps the less problematic issue. Concerns about the rapidity of the population level changes that gene drives can effect are essentially efficacy-based concerns. Such concerns are not ethical in nature, but instead intuitions about risk or harm. Concerns about rapidity or efficacy perhaps reflect anxieties about the reversibility, or irreversibility, of a population level change and our ability to track its consequences. Where the effects of population alteration slowly become clear over many hundreds of generations in the context of selective breeding, there is ample time to collect and study the relevant data and understand the changes that are brought about. This in turn allows a sufficiently large window of opportunity to halt, modify or reverse those changes where we come to realise that they bring about undesirable consequences. For gene drive technologies however, given the much shorter time in which population level changes are effected, this window of opportunity for harm

prevention is significantly reduced. Thus, there are good reasons to be concerned about the rapidity or efficacy and potential irreversibility of gene drives from a risk perspective. This a concern not inherently ethical in nature and is discussed in Part Three.

Turning to the 'Unnaturalness' concern, we might note that the natural versus unnatural dichotomy is not as strict as it appears at first blush. As the Nuffield Council on Bioethics suggest, the dividing line between conventional breeding techniques and genetic technologies is not as bright as many argue – in the context of plants and insects, many otherwise foreign traits have been introduced not by genetic technologies but by other techniques, such as radiation.[84] Thus, whilst it is true that in public consultations concerns regarding the 'unnatural' are widely noted as the most vexing, public mistrust does not always have at its core substantive or easily rationalised moral intuitions.[85] Further, whilst public concerns might be stirred by the introduction of the genetic material of one species into the genome of another, this anxiety does not reflect our empirical understandings of the way genetic material exists and moves within and without species boundaries in the wild. There are many instances in which the genetic material of different species is combined within an organism without any human intervention at all; in viruses, human and animal DNA are combined all the time.[86]

In respects to gene drive technologies specifically, the *Wolbachia* drives that disrupt reproductive pathways in insects are brought about by the insertion of the *Wolbachia pipentis* bacterium into the target species. This phenomenon was first observed in nature, and some estimates now suggest that *Wolbachia* bacteria has infected over three quarters of the planets wild-type insect species without any human intervention at all.[87] Thus, when we point to concerns regarding the 'unnatural' in the context of objecting to gene drive technologies and do so by

[84] Nuffield Council on Bioethics, Genetically Modified Crops: The Ethical and Social Issues 1999 34.
[85] Ibid 34.
[86] Albert Weale, 'Ethical Arguments Relevant to the Use of GM Crops' (2010) New Biotechnology 583, 585.
[87] Kozek and Wieslaw 'The Discovery of Wolbachia in Arthropods and Nematodes – A Historical Perspective' in Hoerauf and Rao (eds) *Wolbachia: A Bug's Life in Another Bug* (Karger 2007).

distinguishing them from more traditional selective breeding techniques, it is somewhat difficult to discern what value it is that we are so concerned to safeguard. For these reasons, it is suggested here that population alteration drives are no more ethically problematic than the selective breeding techniques we have used for many centuries.

This section and the last assessed whether there is an intrinsic moral prohibition pertaining to the use of gene drives technologies. That is, these sections asked whether there is any moral prohibition on the use of gene drive technologies that obtains in all cases, from either an environmental ethics or animal rights perspective. Additionally, the analysis above pulled out some of the conditions under which the use of gene drive technologies might well be ethically problematic. Oftentimes, these contingent concerns reflected novel intuitions about harm.

3. From Ethics, to Framing and Regulatory Decision Making

Taking account of the discussions above, I conclude that there are no *intrinsic* moral concerns regarding the use of gene drive technologies from either an environmental ethics or animal rights perspective. Whilst this conclusion is somewhat surprising, it is a far cry from giving gene drive technologies the ethical green light. Whilst there may be no intrinsic ethical concerns surrounding the use of gene drive technologies, the contingent ethical concerns are varied and many. The thick description rendered by the ethical enquiries pursued above demonstrates that there is an awful lot more to think about in developing an understanding of gene drive technologies than the application of technical expertise would have us believe. The analysis above demonstrates that the arguments do not run just one way – this is not just a question of a moral duty to rescue, through technological means. Instead, there are contingent concerns governing the ethical permissibility of genes drive technologies, the elucidation of which teach us much about the range of implications that the technology might have. For the most part, these contingent concerns depend on the use to which the gene drive is put, either because of the particularities of the species that it affects or the nature and properties of the modifications it instantiates. In this way, I demonstrate the

importance of ethics in a building frames for understanding novel technologies that extend beyond technical expertise alone.

Drawing some initial conclusions on the ethical qualities of gene drive technologies is important for a variety of reasons. First, and arguably most importantly, for the sake of right conduct and good ethical practice it is important to know how and when any given course of conduct offends ethical or moral principles. If regulation aspires to good ethical practice, as most regulation does, then understanding the ethical qualities of the proposed course of conduct it vital.

Secondly, understanding whether a proposed course of action is ethical serves as a good indicator of what public opinion might be. That is not to say that the general public is constituted of fully-fledged ethicists, or that I am advocating for some sort of ethics by consensus. Rather, it is the more modest claim that, all things being equal, publics are more likely to denounce or resist unethical practices than they are ethical ones. For those reasons outlined in Chapter Five, public opinion can have serious and far-ranging implications for regulatory efficacy and thus, whilst I am not advocating for regulation by popular opinion, it ought not be ignored.

Thirdly, the ethical enquiry engaged in above places a number of overflows that would otherwise be overlooked within the frame that we build in order to better understand the use and regulation of gene drive technologies.

For example, where a gene drive proposes to alter a population of a species with highly complex social behaviours, we should pause to consider the relational implications that such a drive would have as a tool for identifying novel harms beyond harms to human health and/or the environment. In the absence of significant benefits to public health, we should have pause to consider whether pursuing such an application of the technology is an impermissible demonstration of hubris.

The contingent, or extrinsic, concerns that were identified above can oftentimes be distilled down to more conventional questions of harm, but harms that would otherwise be left outside of

the frame that we build for these technologies. As such, I propose some insights into how these issues might be navigated, and how they might be taken account of in regulatory decision making.

It is precisely because many of the extrinsic concerns explored above reflect intuitions around harm, or overflows, that they ought to be taken account of in the frame that we build. The ways such considerations might feed into the regulatory process are various. First, some extrinsic concerns may provide reasons to prohibit the development and deployment of certain gene drive technologies altogether. These reasons might attach to the purpose for which the drive is developed, or the overflows it will bear for the target or other species. With regard to the former, for example, a proposed use of gene drive technologies for aesthetic purposes, such as fixing a rare coat colour within the population, might well be refused regulatory approval once the lack of health or environmental benefits have been balanced against the subsisting concerns regarding instrumentalization of the species or human overreaching in the pursuit of mastery. Returning to a point made earlier, many of the enquiries in this respect will engage with questions regarding the legitimacy of the research imperative, or the value of research.[88]

With regard to the latter, the relational concerns contingent upon the target species' capacity for sociality and some primitive cognition might prevent the use of gene drive technologies in species bearing the sorts of properties we look for. For instance, if it were the case that a legitimate need to reduce an elephant population existed, the fact that a gene drive solution would damage social structures and hierarchies over many generations leading to resource scarcity and community conflict, which would in turn cause starvation and suffering, might well provide regulators with cogent ethical reasons to prefer more traditional methods of population control which, all things considered, would cause less suffering. In these ways then, some of the contingent concerns or overflows scoped above might aid decision makers with regard to the binary decision to prohibit or authorise the use of gene drive technologies.

[88] Maria Lee, 'Beyond Safety? The Broadening Scope of Risk Regulation' (2009) Current Legal Problems 242.

Second, some of the extrinsic concerns raised above serve an important function in highlighting to decision makers the harms, beyond conventional accounts of suffering, that we might have cause to worry about. In this way, these ethical enquiries play an important role in identifying overlooked overflows and so avoiding the pitfalls of 'ignorance' common place within decision making for areas of high technological complexity.[89] Concerns about ignorance are pertinent across a range of complex technologies and activities, ranging from the use of pesticides to nanotechnology, and is of no less concern in the gene drive context.[90] If ignorance in decision making reflects concerns that 'we don't know what we don't know' then some of the issues explored above may well help to expand the bounds of our understanding and knowledge by articulating the sorts of questions that we ought to ask of ourselves in respects of more novel harms. For instance, discussing the implications of a relational account of moral status raised a number of questions for technical experts. Identifying and answering these questions pushes back the bounds of our knowledge revealing a pathway to overflows that might have otherwise been unanticipated. In this way, decision-makers can seek, self-consciously, to overcome ignorance and build better frames. By acknowledging the possibility of novel harms or interests, we might better enable ourselves to gather the relevant information or data, capable of confirming or assuaging such concerns. This in turn might affect decision outcomes (whether a certain use is or is not approved) or may be used to help inform what conditions ought to be placed on an approval. For instance, the existence of contingent concerns regarding whether a genetic change causes harm to the target organism, or to its environment, might direct decision makers to demand further research in one particular direction, prior to granting permission for the technology's use or make data collection on that issue a condition of approval.

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[89] B Wynne, 'Uncertainty and Environmental Learning: Reconceiving Science and Policy in the Preventive Paradigm' (1992) *Global Environmental Change* 111. For an alternative framework of risk, uncertainty and ignorance, see: V Walker, 'The Siren Songs of Science: Toward a Taxonomy of Scientific Uncertainty for Decisionmakers' (1991) *Connecticut Law Review* 567.

[90] Rebecca Dresser, 'Building an Ethical Foundation for First In-Human NanoTrials' (2012) Journal of Law and Medical Ethics 802.

In this way then, we ought to conceive of ethical enquiries as vital to the building of robust frames and conditioning the sorts of questions we ask of ourselves as lawyers and regulators. The ethical enquiries engaged above, regardless of their conclusion as to the ethical qualities of the proposed technology, play a significant role in expanding the range of knowledge claims we consider relevant.

CHAPTER SEVEN: GENE DRIVE & EXPLOITATION

In the literature concerning clinical research ethics and bioethics more generally, much has been written about paternalism, abuse, neglect, benevolence and non-maleficence.[1] These concepts, in one guise or another, are considered guiding principles in the practice of health care and the formulation of health policy. For the most part, consensus has been achieved with regards to both a definitional and normative understanding of each of these concepts. However, the contention here is that these categories of concern are not capable of articulating the wrongs that we might have reason to think about in the context of both experimental research into the use of gene drive technologies and the deployment of gene drive technologies beyond the research phase. To try and frame our understanding of gene drives technologies using these concepts in order to describe the possible wrongs that they might generate will fail to render a faithful understanding at all. As such, this Chapter advocates for the use of a theory of exploitation in understanding wrongs to human communities that might occur in the context of gene drive research.

The Chapter takes the following structure. First, I seek to explain why concepts more traditionally associated with similar ethical debates lack descriptive and normative fidelity to the problems that are encountered in the gene drive context. That is, that they fail to provide a suitable frame through which to understand the harms and identify the overflows that might be generated by gene drive technologies. Next, I go on to introduce the leading theory of exploitation before moving on to think about the ways in which such a theory is both useful and resonant in the gene drive context. The final two sections of this chapter reflect on the ways in which we might use our newfound understanding of the wrongs incurred through gene drive research to prevent harm, as well as noting some of the persisting difficulties that regulators will be required to grapple with.

[1] For examples of this orientation within the bioethical literature, see: Tom L Beauchamp and James E Childress, *Principles of Biomedical Ethics* (Oxford University Press, 7th Edition 2012); Lewis Vaughn, *Bioethics: Principles, Issues and Cases* (Oxford University Press 3rd Edition 2016) and Stephen W Smith and John Coggon et al, *Ethical Judgments: Re-writing Medical Law* (Hart 2017).

1. The Right Wrong

At present, there is a deficient understanding of the wrongs that might be incurred in gene drive research – we cannot articulate them in the language germane to bioethics. They are not acts of unjustified paternalism, they do not constitute violations of human dignity, nor do they lead to the objectification or commodification of the human communities they affect. Failing to engage a proper understanding of the possible wrongs human communities might suffer builds a frame of understanding incapable of capturing all of the harms and overflows that gene drive technologies might implicate. In this way, the ethical enquiry engaged below identifies further overflows to be accommodated within our framing of gene drive technologies.

1.1 Why Not Paternalism?

The scholarly community has a good grasp on what features of a practice or policy make it paternalistic and, further, when paternalism is justified and when it is wrongful. Allen Buchanan, for example, characterizes paternalism as 'interference with a person's freedom of action or freedom of information, or the deliberate dissemination of misinformation.'[2] Similarly, James Childress describes paternalistic action as possessing two facets – the protection or promotion of individual welfare and the attainment of that welfare through the restriction of the preferences, choices or actions of those that they seek to protect.[3] As such, it is widely accepted, that laws requiring any persons travelling in cars to wear seatbelts are paternalistic, but justified nonetheless. Gerald Dworkin describes such a policy as an instantiation of hard paternalism, insofar as it constitutes an infringement of a competent individual's autonomy justified by considerations of that individuals safety and/or welfare.[4] On the other hand, a policy forbidding the sale of junk foods might be considered an instance of unjustified paternalism given that the welfare or health benefit for individuals prevented from consuming these foods cannot be considered sufficient to

[2] Allen Buchanan, 'Medical Paternalism,' (1978) Philosophy and Public Affairs *1* 372.
[3] James F Childress, 'Paternalism in Health Care and Health Policy' in (eds) Richard Ashcroft, Angus Dawson, Heather Draper and John McMillan, *Principles of Health Care Ethics* (Chichester: John Wiley & Sons, 2nd edn 2007) 223.
[4] Gerald Dworkin, *The Theory and Practice of Autonomy* (Cambridge: Cambridge University Press 1988)

merit the autonomy interference that such a policy entails. Thus, for instances of unjustified paternalism, we articulate the harm or the wrong that the paternalistic act inflicts as a fettering of choice or an interference with autonomy interests.

Within the literature concerning the governance or regulation of scientific research, there is a traceable, though now largely discredited strand of thought (emanating particularly from professional regulators) advocating for paternalism within the research setting.[5] The extent to which we can describe any form of research involving humans as paternalistic is doubtful, however doing so does provide certain advantages for researchers. For instance, appeals to paternalism may, in some limited cases, provide justification for what would otherwise be considered less than adequate consenting procedures. As such, researchers may find a degree of freedom in trial design and protocol afforded by appeals to hard paternalism. In consequence, there is a temptation to do away with concerns about gene drive research by stuffing them under the familiar banner of paternalism. However, we cannot describe the deployment of gene drive technologies either in the experimental phase or the proven, post-trial phase, (either with or without the consent of the communities they effect) as acts of paternalism. This is for two reasons. Firstly, paternalistic acts or policies are imposed for the benefit of those whose choice they fetter and there is a lack of certain benefit in the context of gene drive research. Secondly, those enacting paternalistic policies do not ordinarily benefit from the paternalism they enact, but gene drive researchers would benefit from such paternalism.

In the first instance, paternalistic acts or practices are able to identify a benefit accruing to those persons whose autonomy interests they fetter. In the seatbelt example, legislators can point to the reduced instance of mortality for seatbelt wearers involved in road traffic collisions as compared to their seatbelt eschewing counterparts. In the junk food ban example, policymakers can point to reduction in obesity and obesity-related conditions in populations without ready

[5] Ezekiel J Emanuel and Christine C Grady, 'Four Paradigms of Clinical Research and Research Oversight' in Ezekiel J Emanuel, Christine C Grady and Robert A Crouch (eds) *The Oxford Textbook of Clinical Research Ethics* (Oxford University Press 2011) 225.

access to junk foods. In both examples the paternalistic policy provides an easily identifiable and certain benefit. In the case of these paternalistic interventions, there is little question as to whether they will in fact provide a benefit to those whose choice they fetter. In these examples, it is the extent of the benefit, balanced against the extent of the interference with autonomy interests, that calls into question the degree to which the paternalism is justified.

In the context of experimental gene drive releases, the benefits of the technology for the community are heretofore unproven. There is a live question as to whether the release of gene drive technologies *will* benefit the human populations into whose environment they are released. This is because the gene drive may fail to have any effect at all (and thus the human participants neither lose nor gain from the release) or because the gene drive might have unintended adverse consequences for the human participants. In that way there is no sense in which researchers might argue that the release of the gene drive organisms is conclusively for the good of the non-consenting individuals. In the sense that the effects of the release of the drive are as yet unknown, we cannot describe the researcher's activity as paternalistic. Gene drive research poses the possibility of great benefit for the target community, but it also exposes the same community to significant risks of harm – a state of affairs that does not accord with our intuitions regarding ordinary understandings of paternalism of either the soft or hard variety. Therefore, the absence of certain benefits in the context of experimental gene drive releases provides unassailable challenges for a theory of paternalism that finds its moral foundations in the principle of beneficence.[6]

Furthermore, and again putting aside questions of consent, ascriptions of paternalism in respect of experimental drives are inaccurate insofar as the research community stands to gain from the release of gene drive organisms whether or not the release proves effective in reducing disease burden. Alan Wertheimer's leading theory of exploitation (to which we later return) argues

[6] For a thorough explication of the relationship between paternalism and beneficence see: James F Childress, *Who Should Decide? Paternalism in Health Care* (New York: Oxford University Press, 1982).

that the salient feature drawing the dividing line between paternalism and exploitation in most cases is the absence of a benefit accruing to the would-be exploiter.[7] Whereas in instances of paternalism the party fettering the choice of another does not gain from the fettering of choice, in cases of exploitation the exploiter does derive a benefit from the state of affairs he brings about.[8] As such, if arguments as to the relevance of this distinction in the context of gene drive technologies are to succeed, it must first be established that a benefit does accrue to researchers seeking to test their technology in releases affecting human communities.

Following a research trial of any sort, researchers gain a vast wealth of data and knowledge, irrespective of whether the particular intervention that they are researching proves effective. The acquisition of this information cannot and ought not be considered value-free. As Daniel Callahan points out in his careful description of what he calls 'the research imperative' the knowledge acquired through human subject research is valuable in a variety of ways and to a variety of different people.[9] In the first instance, we encounter an Aristotelian pursuit of knowledge for knowledge's sake. The value of this sort of knowledge is said to be shared by all mankind. Second, there is an applied, or instrumental understanding of the value of knowledge – knowledge directed at the attainment of certain ends. This understanding of the value of knowledge identifies the beneficiaries of knowledge advancement as those for whom the knowledge is most valuable. For example, we might say that furthering our knowledge of disease progression in patients with Alzheimer's disease is most valuable to those suffering from the condition, insofar as that knowledge might lead to more effective treatments in future. Finally, there is an understanding of the personal or professional value of knowledge as experienced by researchers. The fact that the knowledge acquired through research involving human participants bears a personal and professional value for the researchers involved has, elsewhere, been described as presenting an

[7] Alan Wertheimer, *Exploitation* (Princeton University Press 1999).
[8] Ibid 208-215.
[9] Daniel Callahan, *What Price Better Health? The Hazards of the Research Imperative* (California: California University Press, 2003).

'intrinsic conflict of interest'.[10] Sharmon Sollitto *et al* have described the conflict between a researcher's primary interests on the one hand and their secondary interests on the other. For example, whilst researchers bear a duty to ensure the integrity of research and the safety of participants – 'primary interests' – they also hold personal interests beyond the scope of their professional duties – 'secondary interests'. Researcher's secondary interests might manifest as concern for their reputation and career advancement,[11] a desire for peer recognition[12] or 'the hope of being the first to fulfil the promise of a new technique'.[13] In part, and as reflected by both Sollitto *et al*, and Daniel Callahan, the existence of these secondary interests is the inevitable consequence of the structure and practices of academic research. In a profession that demands researchers obtain and publish noteworthy findings in order to progress their own careers, the fulfilment of secondary interests is systematically incentivised. Whilst both the practical and ethical dilemmas associated with clinical researchers with vested financial interests are well understood and guarded against, much less attention has been paid to the effects of non-financial interests. This is despite the fact that some of the most ethically problematic research carried out in the twentieth century was notably devoid of any discernible financial interests on the part of the clinicians or researchers involved. In their recounting of the hazards of non-financial interests in research, both Norman Levinksy and Richard Saver separately note the absence of any financial interests held by the researchers in the Tuskegee Syphilis Study,[14] the Jewish Chronic Disease

[10] Sharmon Sollitto, Sharona Hoffman, Maxwell J Mehlmann, Robert J Lederman, Stuart J Youngner and Michael M Lederman, 'Intrinsic Conflicts of Interests in Clinical Research: A Need for Disclosure' (2003) Kennedy Institute Ethics Journal 83. See also: Norman G Levinksy, 'Non-financial Conflicts of Interests in Research (2002) New England Journal of Medicine 759.

[11] Sollitto et al (n10) 85.

[12] David Korn, 'Conflicts of Interest in Biomedical Research' (2000) Journal of the American Medical Association 2234, 2234-7.

[13] Sollitto et al (n10) 85. For an elucidation of the influence of this particular 'secondary interest' see: Bernard Lo, Leslie E Wolf and Abiona Berkeley, 'Conflict of Interest Policies for Investigators in Clinical Trials' (2000) New England Journal of Medicine 1616.

[14] Charlotte Paul and Barbara Brooks, 'The Rationalization of Unethical Research: Revisionist Accounts of the Tuskegee Syphilis Study and the New Zealand "Unfortunate Experiment"' (2015) American Journal of Public Health 12.

Hospital Case[15] or the Kennedy Krieger Institute Lead Paint Study.[16] As such, in the same way that financial interests realised through research constitute a well-recognised and sometimes problematic benefit for researchers, there must also be space within which to appreciate that the knowledge obtained through research can also constitute a benefit, insofar as it is instrumental in fulfilling researchers non-financial interests. In this way then, drawing the distinction between paternalism and exploitation is non-problematic. The benefits to researchers engaging in gene drive research are clear.

This is not to say that all experimental gene drive research within human communities is exploitative by virtue of the benefits accruing to researchers. To meet what Wertheimer calls the 'truth conditions' of an exploitation claim, it must also be shown that the nature of the benefit elicited by the would-be exploiter is sufficient to render the agreement between exploitee and exploiter unfair. The relevance of these other features of an exploitation claim in the context of the deployment of gene drive technologies is a point that we will return to later. However, at this juncture it suffices to say that the existence of the benefit accruing to researchers, in addition to the uncertain benefits for target communities, is enough to quieten claims as to paternalistic endeavour on behalf of researchers involved in experimental releases of gene drive organisms. For these reasons, whilst we might be tempted to do so, we cannot articulate the wrongs of gene drive research as acts of unjustified paternalism.

1.2 Why Not Violations of Human Dignity?

The second temptation when trying to articulate the wrongs that are associated with gene drive research would be to invoke the language of human dignity. The growth of concern for human dignity is apparent in the human rights context generally with a range of international rights based

[15] See: John D Arras, 'The Jewish Hospital Chronic Disease Case' in (eds) Ezekiel J Emanuel, Christine C Grady, and Robert A Crouch, *The Oxford Handbook on Clinical Research Ethics* (Oxford: Oxford University Press, 2008).
[16] David R Buchanan and Franklin G Miller, 'Justice and Fairness in the Kennedy Kreiger Institute Lead Paint Study: The Ethics of Public Health Research on Less Expensive, Less Effective Interventions' (2006) American Journal of Public Health 781.

instruments acknowledging and upholding the value of human dignity explicitly.[17] Furthermore, concern for human dignity has developed a growing purchase in debates surrounding life sciences research and the use of genetic technologies particularly. [18] For example, the Council of Europe's Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine explicitly notes the need to uphold human dignity in the scientific context.[19] As such, we might ask ourselves whether any wrongs committed in the context of gene drive research can be articulated as violations of human dignity.

The concept of dignity in bioethics has been hard to pin down; Jacob Dahl Rendtorff and Peter Kemp, for instance, offer no fewer than six understandings of human dignity.[20] The debate around what human dignity actually is has been fierce, and in finding no satisfactory answer some have been lead to declare it a useless concept.[21] For our purposes here, I suspend judgement on the utility or coherence of dignity as a guiding value in bioethics and instead ask whether it might, whatever shape it takes, be relevant to gene drive research. Given dignity's many faces and functions, it is useful to proffer some of the dominant understandings before assessing its relevance.

Tracing the use of 'dignity' across a range of international legal instruments, as well as the judgments of the European Court of Human Rights, Beyleveld and Brownsword suggest that human dignity reaches beyond individuals and is, instead, a constitutive value of the societies within which we live.[22] As such, where the choices or preferences of groups or individuals do not accord with the communally held value of human dignity, they are 'simply off limits'.[23] For

[17] For instance see: United Nations, *Universal Declaration of Human Rights* (Geneva: UN, 1948).
[18] Not only in the context of concern for the dignity of those subject to gene editing, but also concern for the dignity of those performing gene editing.
[19] Council of Europe, *Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine*. (Strasbourg: Council of Europe, 1997).
[20] J D Rendtorff and P Kemp, *Basic Ethical Principles in European Bioethics and Biolaw*, *Vol I-II* (Barcelona and Copenhagen: Institut Borja di bioètica and Centre for Ethics and Law 2000).
[21] Ruth Macklin, 'Dignity Is A Useless Concept' (2003) British Medical Journal 1419.
[22] Deryck Beyleveld and Roger Brownsword, 'Human Dignity and the New Bioethics: Human Dignity as Constraint' in (ed) Deryck Beyleveld, *Human Dignity in Bioethics and Biolaw* (Oxford: Oxford University Press 1993).
[23] Ibid 29.

Beyleveld and Brownsword then, the concept of human dignity is one of constraint. In this way then, we are able to make sense of the *Conseil d'Etat's* prohibition on consensual dwarf-throwing[24] and the German Court's refusal to grant a licence for a mechanical peep-show.[25] Adam Schulman traces the sources of human dignity back through the human rights legislation and national constitutions of the twentieth century, through Kantian moral philosophy, biblical religion and classical antiquity.[26] Having 'untangled' the sources of human dignity, Schulman contends that its value ultimately reflects the 'essential, inviolable core of our humanity'.[27] Schulman's argument seems to suggest that those things that make us vulnerable, flawed, yet ever hopeful mortals are the very things at stake in the context of various biotechnological advances. For Schulman then, paying due respect to human dignity is about conserving the features of our very humanity. However, contrary to the two accounts explored above, a considerable strand of thought within contemporary bioethics considers human dignity nothing more than a proxy for pre-existing norms. Ruth Macklin for instance, describes human dignity as a mere slogan which, at its base, means nothing more than respect for autonomy and respect for persons. Macklin's claims are further supported by the recent literature concerning human dignity that explicitly foregrounds the centrality of autonomy in theories of human dignity.[28] Furthermore, such claims as to synonymy between dignity and autonomy are unsurprising given that many scholars trace human dignity into the works of Kant, for whom autonomy played an essential role in explaining the distinctive nature of human dignity. It ought to be noted however, that whilst many aspects of the dignity-as-autonomy argument are compelling, they are not without challenge. Mary Ford Neal challenges

[24] *Manuel Wackenheim v France*, Communication No 854/1999, U.N. Doc. CCPR/C/75/D/854/1999 (2002).
[25] BVerGE 64, 274-Peep-Show (1981).
[26] Adam Schulman, 'Bioethics and the Question of Human Dignity' in (eds) Edmund D Pellegrino, Adam Schulman and Thomas W Merrill, *Human Dignity and Bioethics* (University of Notre Dame Press, 2009) 3-18. Note, Beyleveld and Brownsword also observe the centrality of Kantian moral philosophy to understandings of human dignity. At the end of the Chapter Two they make the case explicitly for more Kantian thinking in the legal and moral philosophical literature surrounding human dignity.
[27] Schulman (n26) 17.
[28] For instance, see: Luís R Barroso, 'Here, There and Everywhere: Human Dignity in Contemporary Law and in the Transnational Discourse' (2012) Boston College International and Comparative Law Review 35(2) 331; and James Griffin, *On Human Rights* (Oxford: Oxford University Press 2009).

claims of synonymy, suggesting that if they were indeed true, we are bereft of an explanation of the 'reflexive' nature of human dignity.[29] If human dignity is just autonomy rebranded, how can it be that in violating your dignity, I '*necessarily and simultaneously* violate my own'?.[30] This valuable challenge aside, there exists a significant body of scholarship that does equate human dignity with nothing more than autonomy and respect for persons and, as such, we ought not exclude this account from our enquiry.[31]

How then, might the release of gene drive technologies implicate any of the three conceptions of human dignity charted above? Attempts to articulate the wrongs that might be committed as 'violations of human dignity' founder when we consider the difficulties we face in determining the ways in the technology actually affects any understanding of the dignity of affected individuals. Whether we adopt Adam Schulman's conception of dignity as 'the essential and inviolable core of our *humanity*'[32] or Deryck Beyleveld and Roger Brownsword's conception of 'dignity as constraint',[33] it is unclear how the dignity of human communities might be implicated by the release of either experimental or tried and trusted gene drive technologies.[34] For the most part, it would appear that any conception of dignity implicated here belongs to the dignity-as-autonomy view, demonstrating concern for the nature and quality of the consent offered up by those individuals into whose environmental gene drive organism are released. As such, where dignity is implicated the questions we might be required to ask of ourselves collapse into the consent-based concerns traversed below.

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[29] Mary Ford Neal, 'Respect for Human Dignity as a 'substantive basic norm'' (2014) International Journal of Law in Context 26.
[30] Ibid 32.
[31] Note that for Beyleveld and Brownsword any claim that human dignity is merely proxy for autonomy is nonsensical given that on their account of dignity-as-constraint, there are a range of situations in which dignity is antithetical to autonomy.
[32] Adam Schulman, 'Bioethics and the Question of Human Dignity' in (eds) Edmund D Pellegrino, Adam Schulman and Thomas W Merrill, *Human Dignity and Bioethics* (University of Notre Dame Press, 2009).
[33] Deryck Beyleveld and Roger Brownsword, 'Human Dignity and the New Bioethics: Human Dignity as Constraint' in (ed) Deryck Beyleveld, *Human Dignity in Bioethics and Biolaw* (Oxford: Oxford University Press 1993).
[34] That is not to say that human dignity is not implicated at all, there are convincing arguments to suggest that development of gene drive technologies constitute an assault on the dignity of those researchers pursuing a Sandelian feats of mastery, see Chapter Two for a further elucidation of arguments along these lines.

2. Understanding Exploitation

This section, and the next, picks up a theory of exploitation and develops an account of its application to gene drive research and deployment. This serves two purposes. In the first instance, it serves to describe the sorts of wrongs that we might have reason to worry about in the context of gene drive research and, secondly, to identify those wrongs that require regulatory intervention. Happily, understanding the nature of the wrong gets us some way toward understanding precisely the regulatory action required to overcome it. In spite of a relatively scant literature, this section suggests that exploitation provides the correct description sorts of wrong that might be committed against individuals and communities during gene drive research. This is not to say that all gene drive research is exploitative, or even that whenever we find that exploitation occurs in a certain research practice that that research ought to be prohibited.

2.1 Why Wertheimian Exploitation?

A range of accounts of exploitation can be found across the moral and political philosophical literature, however, this chapter adopts Alan Wertheimer's account as its start point and the yardstick against which gene drive research is measured. Wertheimer's account has been selected for three reasons. In the first instance, Wertheimer offers an account of exploitation sensitive to the oftentimes non-ideal conditions within which it operates.[35] As such, an application of Wertheimer's account is careful to avoid feats of wishful thinking or moral perfectionism that cannot provide solutions to real world regulatory quandaries. Secondly, Wertheimer's account avoids taking any position on the relative merits of Marxism or liberalism – a debate that has dogged previous accounts of exploitation in their application to real world phenomena.[36] Thirdly, and finally, Wertheimer's account is one friendly to the wants and concerns of any lawyer in the business of seeking solutions to these complex problems.[37] Whilst Wertheimer deftly maps the

[35] Wertheimer (n7)
[36] G A Cohen, 'The Labour Theory of Value and the Concept of Exploitation' (1979) Philosophy and Public Affairs 338.
[37] Such a feature was not confined to Wertheimer's work on exploitation alone, but was a regular feature of his writings praised by I Glen Cohen in an reflection on Wertheimer's career following his death in 2015. See: I Glen Cohen, *Petrie*

moral quality of exploitation, he also provides guidance to the legal responses that such moral features justify or require.

2.2 Explaining Wertheimian Exploitation

Alan Wertheimer's 1996 book, *Exploitation*, provides the most complete theory of exploitation developed to date. Wertheimer's account seeks to identify the concept as it arises in everyday claims and further provide an account of its wrongfulness. As such Wertheimer is interested in understanding whether there is any coherent thread connecting up all of the ordinary language uses of the term 'exploitation' and whether it might tell us anything about the wrongness of exploitation. Further, Wertheimer seeks to locate the wrongness of exploitation as only in doing so, can exploitative agreements be avoided.

This is no mean feat as Wertheimer himself acknowledges the multiplicity of the quite divergent ways in which claims about exploitative transactions, activities or behaviours are deployed in everyday life. It is frequently claimed that hypothetical, commercial organ markets exploit the most socio-economically disadvantaged within society given that the majority of donors hail from the poorest social groupings. Similarly, there is a tendency to think that sex work exploits sex workers[38] and that commercial surrogacy agreements exploit the women offering up their reproductive capacities.[39] In the context of clinical research ethics, we talk about the exploitative nature of placebo-controlled trials in developing countries.[40] Wertheimer uses these common language descriptions, amongst a range of others to highlight the varying form that exploitation claims take.[41] However, despite the fact that these common language claims of exploitation are quite typical in social commentary and debate on these issues, they are somewhat absent in the

Flom Law Blog 'Remembering Alan Wertheimer: Not Only a Philosopher But a Lawyers Philosopher' April 20th 2015, http://blog.petrieflom.law.harvard.edu/2015/04/20/remembering-alan-wertheimer-not-only-a-philosophers-philosopher-but-a-lawyers-philosopher/ Last Accessed 15th June 2019

[38] Vanessa E Munro, 'Exploring Exploitation: Trafficking in Sex, Work and Sex Work' in Vanessa E Munro and Marina Della Giusta (eds) *Demanding Sex: Critical Reflections on the Regulation of Prostitution* (Routledge 2008).

[39] Stephen Wilkinson, 'The Exploitation Argument Against Commercial Surrogacy' (2003) Bioethics 169.

[40] Jennifer S Hawkins and Ezekiel J Emanuel, *Exploitation and Developing Countries: The Ethics of Clinical Research* (Princeton University Press 2008).

[41] Wertheimer (n7) 3-5.

legal and philosophical literature concerning the same debates. As noted above, in debates both for and against commercial organ markets the wrongfulness of the proposed course of action is often derived from concerns for objectification or commodification rather than exploitation.[42] The same is also true of debates surrounding the moral and legal permissibility of sex work and commercial surrogacy.

With regard to commodification, we cannot claim that releasing experimental gene drive-edited organisms into the environment of any given community, either with or without their prior approval, leads to any sort of commodification as commodification necessarily entails reducing a thing to its cash equivalent and making it the object of a commercial transaction. As such, we cannot say that gene drive researchers are 'commodifying' the communities that they interact with. Nor can we claim that to do so objectifies members of those communities because, at least to some extent, researchers are treating members of the communities as more than just things or a means to an end, precisely because the community itself stands to benefit from the safe and effective release of gene drive technologies that the research is aiming toward. Alternatively, scholars seek to ground the wrongfulness of each of these activities in impermissible violations of human dignity. Proponents of this claim argue that the dignity of those exchanging their organs, sex or reproductive capacities for money, is violated.[43] The extent to which claims about violations of dignity can be conceived of as freestanding from claims regarding objectification has also been a matter of some debate.[44]

Purported conceptual confusion or overlap aside, as argued above, none of these concerns are helpful in articulating the wrongs that might be suffered by either individuals or communities in the context of gene drive research. Any attempts to articulate the wrongs associated with gene drive technologies in these terms provides a deficient understanding of the technology, the way it

[42] See for instance: Kate Greasley, 'Property Rights in the Human Body: Commodification and Objectification' in (eds) Imogen Goold, Kate Greasley, Jonathan Herring and Loane Skene, *Persons, Parts and Property: How Should We Regulate Human Tissue in the 21st Century?* (Hart Publishing 2014).
[43] Calum MacKellar, 'Human Organ Markets and Inherent Human Dignity' (2015) The New Bioethics 53.
[44] Meredith Celene Shwartz, Moral Respect, Objectification and Health Care (Palgrave Macmillan 2019).

is used and its implications for the human communities affected. Given that we cannot articulate the wrongs associated with gene drive research in terms of the traditional bioethical language of unjustified paternalism, violations of human dignity, objectification or commodification we turn now instead to a full account of exploitation in order to provide a full account of the range of overflows generated by gene drive technologies.

2.2.1 Truth Conditions of an Exploitation Claim

a) Benefit to A

Wertheimer notes that in all cases of exploitation, some or other benefit accrues to A as a result of the arrangement entered into with B.[45] The benefit experienced by A plays an important role in distinguishing instances of alleged exploitation from other possible wrongs. For instance, unjustified paternalism, abuse, oppression and discrimination are all wrongs ripe for conflation with exploitation but the boundary is usefully drawn up by reference to a lack of benefit accruing to A in the four former cases. Where A verbally abuses B due to a disagreement about a spilled drink in a bar, it is not necessary for A to benefit from the abuse – quite the opposite, A might in fact suffer quite considerably by the imposition of the criminal law. Similarly, if A refuses to sell B the dog that he is advertising for sale on the grounds of B's party-political affiliation, whilst we might describe the wrong as discrimination, we should be hard pushed to describe it as exploitation.

As such, in order to validate any claim of Wertheimian exploitation, a benefit accruing to A must be identified. The extent of A's benefit need not be particularly large, nor ought the benefit be conceived of in purely financial terms.[46] As Wertheimer points out, the gains accruing to A in the context of commercial surrogacy, student athletes or sex work are all non-monetary but constitutive of an exploitation claim nonetheless.[47] Further, according to Wertheimer, it is not necessary that the gain accruing to A is the mere promotion of A's own self-interest. Instead,

[45] Werthiemer (n7) 17.
[46] Ibid 208- 210.
[47] Ibid 210-211.

Wertheimer adopts what he terms a more 'protean conception' of what does and does not count as a benefit to A. This protean conception is therefore also able to accommodate instances of mediated exploitation, that is, instances in which A exploits B on behalf of another. For example, where a clinician advises a patient to eschew a treatment with proven efficacy in favour of a cheaper, experimental treatment, he exploits B *on behalf* of those individuals who might benefit from the future availability of the cheaper treatment. Although the clinician may not have exploited his patient for his own gain, he has exploited the patient nonetheless and, as such, the patient will have a valid exploitation claim, providing the other truth conditions are met. The ability of Wertheimer's theory to account for the wrongness of 'mediated exploitation' is important in the context of gene drive technologies in particular and we will return to these later when we think about the validity of exploitation claims directed at researchers researching within one community for the benefit of other, future communities.

b) Unfairness to B

Further to A gaining some tangible benefit deriving from the arrangement with B, in order to validate an exploitation claim, the effect of the agreement on B ought to be considered unfair. At this juncture, Wertheimer separates out two different species of potentially exploitative agreements: harmful exploitative agreements and mutually advantageous exploitative agreements.

Harmful exploitation describes an agreement that, at best, benefits A whilst failing to benefit B and, at worst, benefits A whilst also causing some material suffering to B. In the case of the former – failure to benefit B – the wrong suffered by B here is by means of his instrumentalization by A. As Allen Buchanan has put it, B suffers 'the harmful, merely instrumental utilization of him, or his capacities for one's own advantage, or for the sake of one's own ends."[48] In the context of that later example – material suffering on the part of B – the harm is tangible and readily

[48] Allen Buchanan*, Ethics, Efficiency and the Market* (New Jersey: Rowman and Allanheld 1985) 87.

identifiable. For example, where B is enslaved by A, we can straightforwardly recognise the associated maltreatment and fettering of freedoms as a harm.[49]

In this way, Wertheimer appears to locate the unfairness of the agreement *in* the harm incurred by B. That is to say, according to Wertheimer, what makes harmful exploitation unfair is the very harm that B suffers as a result of the agreement. However, early on in his exegesis of what fairness demands in the context of a mutually advantageous agreement or transaction, Wertheimer notes that there is likely no 'non-problematic theory of fairness' available to be straightforwardly applied.[50] Nonetheless, Wertheimer scopes several suggestions, many drawing on insights garnered by behavioural economics.[51] Wertheimer considers, and in turn dismisses, accounts of fairness in mutually advantageous exploitation grounded in rational bargaining theory, equality and comparison with competitive and non-competitive markets.

Ultimately, Wertheimer contends that conditions of fairness in mutually advantageous agreements might be discerned by reference to the conditions that a hypothetical market would demand.[52] At least in part, Wertheimer's reliance on the 'price' or conditions required by a hypothetical market appear to reflect the idea that the hypothetical market imagines both parties to the agreement to be well informed and unpressured. In this way then, the hypothetical market stipulates a price or conditions to the agreement that would be amenable to a well informed and unpressured agent. As such, whether the price or conditions attached to an agreement are fair is, to some extent, a function of the information and the freedom-related conditions of the particular agent's party to the agreement. This view is reinforced when, later in the chapter, speaking of competitive markets from which hypothetical markets are derived, Wertheimer notes:

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[49] Note, Nigel Simmonds might well suggest that the sorts of slavery encountered in ancient Greek and Roman civilizations did not as a matter of course involve any maltreatment or, indeed, any fettering of the range of valuable freedoms available to the slave. As such, Simmonds might be more likely to conceive of particular instances of slavery as more akin to mutually advantageous exploitation discussed below, rather than instances of harmful exploitation as we conceive of it here. See: Nigel E Simmonds, *Law as a Moral Idea* (Oxford University Press 2012) 100-102.

[50] Wertheimer makes this claim across the range of his work. For the most recent explication of this concern in writing prior to his death, see: Alan Wertheimer, *Rethinking Clinical Research Ethics: Widening the Lens* (Oxford: Oxford University Press 2011) 210.

[51] Wertheimer (n7) 227-236.

[52] Ibid 232.

> Still, even though a competitive market price does not reflect a deep principle of justice, it does reflect a crucial moral dimension of the relationship between the parties to the transaction. The competitive market price is a price at which neither party takes special unfair advantage of particular defects in the other party's decision making capacity or special vulnerabilities in the other party's situation. It is a price at which the specific parties to the transaction do not receive greater value than they would receive if they did not encounter each other.[53]

In this way then, three things are apparent with regard to Wertheimer's understanding of fairness within potentially exploitative, mutually advantageous agreements. Firstly, the nature of the relationship between the parties has a bearing on the moral quality and fairness of the agreement subject to scrutiny.

Secondly, as claimed above, various aspects of the agent's decision-making capacity are also relevant to the fairness of the proposed agreement. At minimum, we should have concern for the information each party is equipped with. Further, we might also have regard to each party's understanding of their counterparts' informational position. For instance, it might be fairness-affecting if A knows B to lack a crucial piece of information and/or understanding that, were they in receipt of, would cause them to act differently. By way of example, if it were the case that B was labouring under a misapprehension as to the actual competitive market price of whatever was subject to the transaction, and A knowing of that mistake seeks to transact with B on the basis of that mistake, we might ordinarily consider A to have taken unfair advantage of B. In addition to the role that information plays, we might also have regard to B's ability to choose to do otherwise. Thus, Wertheimer requires us to pay attention to both the knowledge and situational vulnerabilities of the parties when considering whether the agreement can be said to be fair.

Finally, the suggestion that fairness obtains when the parties to the transaction do not receive greater value than they would receive if they did not encounter each other suggests that some counterfactual analyses might help in determining whether an agreement that benefits both parties is or is not fair. For instance, we might ask whether A is better off transacting with B than any other party that might seek to enter into such an agreement. Perhaps, if the particularities of either B or B's situation enhance A's gain in a way that is not observed with respect to other willing

[53] Ibid 232.

parties, unfairness within the agreement can be identified. This last point raises a question with regard to gene drive technologies that we will return to later in this Chapter when we analyse the ways in which exploitation might be relevant in the research context. For now, it suffices to note that we will return to ask whether gene drive research carried out in a particular population can be said to be exploitative by virtue of the fact that there exists another less vulnerable population within which the research might be conducted instead.

c) Role of Consent

Once Wertheimer has scoped the need for a gain to A and unfairness to B in order to satisfy the truth conditions of an exploitation claim, Wertheimer turns to address the role that consent might play in claims about exploitation. Wertheimer's concern here is two-fold. In the first instance, he seeks to argue that exploitation can take place, both with and without B's consent to the agreement. As such, in Wertheimer's view, the presence or absence of consent will not affect the truth conditions of an exploitation claim. Second, he seeks to demonstrate that the presence or absence of consent has implications for the moral quality of the agreement in question, as well as having implications for the legal responses that the exploitation necessitates. Therefore, whilst consent plays no role in determining whether an agreement is exploitative or not, the presence or absence of consent will play a role in prescribing the correct legal response to the exploitative agreement.

In short, Wertheimer suggests that in the majority of cases of consensual exploitation, attempts by the state to prohibit the agreement or interfere with its conditions cannot be justified. Further, because according to Wertheimer the presence or absence of consent has implications for state responsibilities *viz a viz* exploitative agreements, it is important for him to provide some elucidation of those situations in which although consent is provided, it is said to be vitiated by some other factor or factors.

As such, Wertheimer considers those factors that represent a defect in consent due to some detrimental alteration in B's decision-making capacity and those factors that represent a defect in consent due to some unfavourable features of B's objective situation. In this way then, Wertheimer

divides up the possible causes of defective consent in much the same way as other exploitation theorists, such as Michael Gorr's analysis of what he calls 'incapacity-exploitation' as compared with 'circumstantial-exploitation'.[54]

Wertheimer himself pays little attention to describing the sorts of deficient decision-making capacity that might be sufficient to render any given instance of consent defective. Given the wealth of literature treating such questions, this is not in and of itself problematic. Various different theories of the cognitive and informational capabilities of decision-making agents provide satisfactory answers to this question.[55] The somewhat greater challenge lies in stipulating the features of B's objective situation sufficient to render B's consent defective.

In many ways, the challenge faced by Wertheimer in this connection is one that has challenged a great number of moral philosophers considering the conditions under which we might ascribe responsibility to an agent.[56] In charting the features of B's objective situation that might render B's consent defective, Wertheimer considers three possibilities: false consciousness, inequality of bargaining power and hard circumstances. Ultimately, Wertheimer concludes that none of these features, if found to be a part of B's objective situation, can be said to constitute a defect in consent. That is not to say that they cannot *give rise* to defective consent – and this is perhaps where the already close connection between B's objective situation and B's epistemic position and capacity for voluntariness is drawn even tighter. The precise implications that the consent requirement has for determining whether any given instance of gene drive research is or is not exploitative will be returned to in Section Five.

d) The Relevance of Background Injustices

[54] Michael Gorr, *Coercion, Freedom and Exploitation* (Peter Lang Publishing, 1988) 151.
[55] For just one plausible account see: Gerald Dworkin, *The Theory and Practice of Autonomy* (Cambridge: Cambridge University Press 1998), particularly Chapter Seven, Autonomy and Informed Consent.
[56] Note, an increasing number of philosophers pay great attention to the effect that an agent's objective situation plays in both the voluntariness condition and the epistemic condition of moral accounts of agency. For instance, see: George Sher, *Who Knew? Responsibility Without Awareness* (Oxford University Press 2009) and John Martin Fischer and Martin Ravizza, *Responsibility and Control: A Theory of Moral Responsibility* (Cambridge: Cambridge University Press 1998).

Wertheimer's dismissal of unfavourable features of B's objective situation as incapable of rendering B's consent invalid might lead us to think that B's objective situation is never relevant to determinations of exploitation. However, and importantly for our concerns here, that is not the case. Whilst for the most part Wertheimer rejects the suggestion that 'background injustices' experienced by B's might make an agreement between A and B sufficiently unfair as to render it exploitative, there are certain instances in which background injustices that contribute to B's objective situation are relevant. Before we push to consider the instances in which background injustices come to bear on the fairness of an agreement, it is important to note that Wertheimer's concern here is to distinguish between 'taking unfair advantage', which is exploitative, and 'taking advantage of unfairness', which is not.[57] This distinction is important for pragmatic reasons. In the first instance, and as Wertheimer suggests, the distinction serves to articulate the correct target of approbation for B's undesirable circumstances. Where A takes advantage of unfairness experienced by B as a function of background injustices, to attribute moral blame to A occludes the systemic failings of States in respect of the obligations they owe to their citizens. As such, to label the agreement between A and B exploitative under these conditions fails to place the blame at the feet of Governments and, in turn, obscures calls for governments to repair these background injustices.

In essence, Wertheimer argues that placing A on the moral hook in respect of these sorts of agreement stops us placing governments on the moral hook.[58] That being the case, there is a

[57] This is certainly not the view of all philosophers interrogating the concept of exploitation. For instance, Ruth J Sample takes quite a different view. Sample argues 'If we gain advantage from interaction with another, and that advantage is due in part to an injustice he has suffered, we have failed to given him appropriate respect', see: Ruth J Sample, *Exploitation: What It Is and Why It's Wrong* (Rowman & Littlefield Publishers 2003) 74. Sample's account of the wrongness of exploitation is therefore rooted in failures to pay due respect, rather than Wertheimer's account grounded in fairness. That is just one way to account for the divergence of views but a fuller fleshing out of the debate is beyond the scope of the discussion here.

[58] One note of caution here: It is not clear why in cases of 'taking advantage of unfairness' a label of exploitation necessarily precludes placing those Governments that fail in their obligations to citizens on the moral hook. As Wertheimer himself notes in Chapter 9, 'there is plenty of responsibility to go around' p.293. On Wertheimer's own view, moral hooks can, and do accommodate more than one morally blameworthy party, even where their conduct is blameworthy in different ways or for different reasons. He makes this point with respect to the wrongs committed by both A and B when they enter into an exploitative agreement. 'Just as B's consent to an exploitative transaction with A does not get A off the moral hook, that A acts wrongly in exploiting B does not necessarily get B off the moral hook.' p.293-294. As such, it is not apparent why describing A's conduct as exploitative, and therefore attributing a

pragmatic argument for distinguishing between 'taking unfair advantage' and 'taking advantage of unfairness' if our primary concern, all things considered, is an overall improvement in B's objective situation. However, the practical implications of distinguishing between 'taking unfair advantage' and 'taking advantage of unfairness' aside, there are circumstances under which, according to Wertheimer, the background injustices bearing on B's objective situation will be relevant to determinations of exploitation. Later in this chapter, we turn to consider the possibility of exploitation in research taking place in developing countries where background injustices are rife and so it serves well to linger on Wertheimer's argument here. For Wertheimer, unless A is causally responsible for the background injustices he takes advantage of, or owes special obligations of repair in respect of those background injustices, A will be said to be taking advantage of unfairness, therefore placing the agreement between A and B beyond accusations of exploitation.

Therefore, determining whether A is taking unfair advantage of B, and therefore exploiting B, requires an understanding of A's obligations with regard to B's objective situation (of which background injustices are a part). Wertheimer does not offer any contemplation of situations in which these conditions obtain, but they are not hard to imagine. For instance, imagine A is responsible for food distribution networks in an area afflicted by famine. A worsens the situation of the local population in respect of their starvation by allowing the available foodstuffs to spoil on the back of trucks before it is distributed.[59] Observing the now further increased food scarcity, A increases the price of the foodstuffs to well beyond the already prohibitively high competitive market rates. In such a case we might straightforwardly say that A bears causal responsibility for worsening the background injustices that they take advantage of. Therefore, we can conclude that the sale of food at extortionate rates by A to B is exploitative. Furthermore, it takes little to imagine

moral wrong to A prevents us rendering a moral evaluation of the relevant state's failure to repair the background conditions that make these sorts of agreements possible, or even likely.

[59] It is not clear whether A must fail in his obligations *viz a viz* background injustices intentionally, or through recklessness or negligence in order to lay the basis for a later claim of exploitation where A seeks to take advantage of the background injustices he has contributed to. However, such an analysis is beyond the scope of the discussion here and so it assumed that contribution to background injustices or failure to repair them as a result of any degree of fault is sufficient.

a similar situation in which A does not just worsen the background injustices, but is instead the cause of them.

Whilst thinking about the ways in which an alleged exploiter might be considered causally responsible for contributing to background injustices is uncomplicated, understanding what it means to have an obligation to repair background injustice is less straightforward. Wertheimer offers little instruction as to who might owe these obligations and, further, how they might be grounded. One solution is to adopt the position David Miller adopts in *Distributing Responsibilities.*[60] Miller's 'connection theory' argues that individuals have special obligations to repair bad situations when one of the following obtains: the agent is causally responsible for the bad condition; the agent is morally responsible for the bad condition; the agent has the capacity to remedy the bad condition; or the agent has a communal obligation to the affected party or parties. Following the lead of Daniel Butt, one might go even further (and somewhat problematically so for our purposes) and suggest that individuals have obligations to remedy background injustices whenever they benefit from them.[61] Miller's account of special obligations to repair background injustices provides an expansive view placing a majority of alleged exploiters within its ambit, whilst Butt's account covers all would be exploiters by virtue of its focus on benefit or gain. Alternatively, we might instead focus on more formal ascriptions of such obligations and thus a more restrictive account. For instance, we might conclude that only those persons formally assigned these sorts of obligations by virtue of their institutional responsibilities are liable to discharge them. As such, and as Miller points out, on this view, if we were to ask who owes reparative obligations in respect of a child educationally disadvantaged due to their social economic status (constituting background injustice) we might point to a social worker, a schoolteacher or even a local politician.

In the context of clinical research specifically, Wertheimer says the following with regard to background injustices and the possibility of taking unfair advantage:

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[60] David Miller, 'Distributing Responsibilities' (2001) The Journal of Political Philosophy 453
[61] Daniel Butt, 'On Benefitting From Injustice' (2007) Canadian Journal of Philosophy 129.

> If clinical researchers take advantage of the unjust background conditions in which people in developing societies find themselves, it does not follow that they are taking unfair advantage of the people. They may or may not be doing so. To say that they are taking unfair advantage of the people, it must be shown that researchers have a specific—not general humanitarian— obligation to provide more to their research participants than they are actually providing. [62]

Whether we adopt a moral philosophical account of obligations to repair background injustices, or chose an account instead rooted in existing social and institutional practices, it is clear that *some* account is required in order to make sense of Wertheimer's claims regarding the relevance of background injustices. As indicated above, questions regarding the relevance of background injustices are crucial to understanding when gene drive research might be considered exploitative. As such, when we return to examine the instances in which gene drive can be conclusively considered exploitative, an account of the researcher's obligations in respect of host communities will be required and the background injustices that form part of the objective situation will be considered.

Asking questions about the background injustices affecting communities earmarked for the release of gene drive technologies is vital to understanding the technology and its implications (and therefore how our frames ought to be constructed). Only when we understand what background injustices (if any) obtain, can we be in any position to make meaningful predictions about what overflows the deployment of gene drive technologies might generate. For example, if target communities are afflicted by high rates of poverty, poor access to healthcare and almost non-existent infrastructure, their position is radically different to that of communities facing the release of gene drive technologies where access to health care is good, monitoring infrastructures are in place and the mobilization of resources required by means of emergency response is possible. Outcomes for communities within which gene drive technologies are released will be qualitatively different and materially better or worse, depending on the prevalence or absence of background injustices affecting their objective situation. In this way, these factors – most of which cannot be

[62] Alan Wertheimer, 'Exploitation in Clinical Research' in (eds) Emanuel J Ezekiel, Christine Grady, Robert A Crouch, Reidar K Lie, Franklin G Miller and David Wendler, *Oxford Handbook of Clinical Research Ethics* (Oxford: Oxford University Press 201) 205-206.

identified or reconciled by technical expertise – play a significant role in determining the fairness of the transaction posed, and therefore whether or not any wrong might be committed, or overflow generated.

2.3 Moral Force & Moral Weight of an Exploitation Claim

All that has gone above provides the 'truth conditions' required for the validation, or rejection of an exploitation claim. If all of the conditions are satisfied, then we can say that the agreement existing between A and B *is* exploitative. But then what? Ought the State intervene to prohibit all exploitative agreements, or only some? Instead of outright prohibition of exploitative agreements, ought the State instead demand changes in certain conditions of the agreement? Or, should States refrain from interfering with such agreements, for fear of illegitimate interference with the autonomy interests of parties making private agreements? In his explication of the moral weight and moral force of exploitation, Wertheimer provides a framework for answering these questions. Whilst moral weight describes the extent of the wrongness of the exploitative agreement, moral force describes the legal responses that an exploitative agreement necessitate. Wertheimer is clear that the moral force of either harmful or non-consensual exploitation is sufficient to require outright legal prohibition.[63] However, and as has been the case throughout this analysis, the picture is less clear with respect to mutually advantageous and consensual exploitative transactions. In Wertheimer's view, and, in fact the view of many others, there are sometimes good reasons to allow these sorts of transactions to take place. For instance, if it is the case that B is better off following an exploitative transaction than they would be if their transaction were never to take place, then we ought not to remove from B the option to better his own position. Furthermore, whether or not B is actually in a better position than he would otherwise have been in the aftermath of the transaction, to prohibit the transaction would constitute an unjustified interference with his autonomy interests. After all, according to some, the law is not regularly in the business of stopping

[63] Wertheimer (n7) 347.

those that it governs from making bad choices for themselves. Wertheimer's claim, contrary to the likes of Joel Feinberg, is that intervening in certain mutually advantageous, consensual exploitative transactions can be justified by seeking to improve the position of other agents sharing B's situation.[64] Thus for Wertheimer, what he calls 'strategic interventions' are justified because allowing B to be exploited also weakens the bargaining position of other Bs who might also have reason to transact with A. Further, and importantly, these strategic interventions do not necessarily entail prohibitions of exploitative agreements *per se*, but instead seek to alter the conditions of the agreement that render it unfair. As Wertheimer notes:

> On the assumption that it is legitimate for the society to deprive B of the opportunity to enter into a mutually advantageous transaction with A, the legal regime could pursue one of several strategies. It might say, (1) If we find that the terms are unfair, then A will get nothing, (2) If we find the terms are unfair, then we will determine what A will get, or (3) These are the acceptable terms for this kind of transaction.[65]

Still, the questions remain as to which mutually advantageous, consensual exploitative agreements we might ear mark for strategic intervention. Whilst Wertheimer does not speak directly to this issue, some guidance can be gleamed from his work. In the first instance, it is clear that strategic interventions will not be appropriate in situations where A will just choose not to transact with B at all if he is required to adhere to terms of the transaction considered acceptable by society. In this case, the practical effect is to prohibit the transaction thus leaving B worse off than he would have been should the transaction have gone ahead. For example, strategic interventions would not be appropriate in the context of agreements taking place under competitive market conditions, as A will likely just choose to transact elsewhere. Secondly, where the intervention stipulating the conditions of the agreement cannot actually improve B's position, there might also be reason to refrain from strategic intervention. In some sense, Wertheimer makes this point explicit when, in distinguishing strategic interventions from other justifications for intervention, such as paternalism or legal moralism, he argues that his position 'seeks ordinary, nonmoral improvements in welfare

[64] Ibid 300-305.
[65] Ibid 302.

for potential exploitees'.[66] Thus, where B's welfare cannot be improved, strategic intervention might be inappropriate.

Wertheimer's arguments with regards to strategic interventions are important for our purposes because they give us pause to think about what we ought to require of researchers at the front line of gene drive research. The argument made here, but fully fleshed out below, is that understanding when an agreement to conduct research within a native community is exploitative, tells us something important about the effects that the research might have on the continuing welfare of Bs, but perhaps even more importantly, it provides some indication about the conditions that we might prescribe for certain agreements in order to maximise the welfare of a class of Bs. Put simply, the claim that I make here, and elaborate on further below, is that paying attention to, and improving the fairness, of the agreements between researchers and target communities can have real practical implications for improving the welfare of the host communities subject to research, as well as improving the safety of research practices themselves. Below, in the elucidation of scenarios we might have reason to consider exploitative, I describe some of the conditions that regulators might impose in order to improve fairness that might in turn improve welfare.

3. When is Gene Drive Research Exploitative?

Now that a full understanding of Wertheimer's theory of exploitation has been laid out, we are in a position to think about the ways in which it might be applicable to gene drive research. This section argues that Wertheimer's theory provides us with a means to identify a range of overflows that conventional, and predominantly technical, understandings of gene drive technologies overlook. In particular, this section argues that there at least three situations in which gene drive research can be said to be exploitative and therefore likely to generate overflows that the regulatory framing of the technology ought to be cognizant of. In that way, the discussion below provides

[66] Ibid 209.

three ethical questions, the answers to which affect our understandings of gene drive technologies and their implications. Firstly, will this application of gene drive research likely face commercialisation? Secondly, can the proposed release of gene drive technologies be considered premature? Thirdly, is there relevant consent supporting this use of the technology?

3.1 Commercialization of Gene Drive Research

There is something of a paradox emerging in the development of gene drive technologies. The initial excitement surrounding Hammond *et al's* breakthrough population suppression drive in 2015 was attributable, in no small part, to the idea that this technology offered something of a silver bullet in the fight against malaria. Unlike vaccination programmes, pesticide spreading and the distribution of bed nets, gene drive technologies offered a 'single use' solution to malaria. What makes the technology so attractive is the claim that malaria might be eradicated within a generation and with the release of a relatively small number of gene drive modified mosquitos. The single use nature of the technology bears several virtues; in the long term the costs of vector control will be reduced, the eradication of malaria will come more quickly than it would with existing techniques and the technology itself is immune to the risk of commercialization. In short, gene drive technologies promised a solution that saves more lives, more quickly, for less money. However, with the virtues enabled by the technology's single use nature come major concerns. The one off, rapid and potentially global effect of the technology is problematic from a risk perspective. When vaccinations or pesticides prove harmful in clinical trials, we simply halt the trial in order to prevent future or further harm. In doing so, further harm to the trial participants is prevented, as is future harm to other individuals to whom the drug might have become available. However, in the context of single use 'global' gene drive technologies this sort of harm prevention is more difficult to achieve. Not only is preventing a drive system from causing further harm to the populations within which it was initially released problematic, but preventing the drive system spreading to and causing harm within new populations is difficult too. As such, a range of legitimate concerns about

our ability to control the technology following release or reverse its effects once harm might be quite straightforwardly identified.

In response to this range of safety-based concerns, scientists began working to develop gene drive technologies that might be both spatially and temporally limited. Their aim was to develop a gene drive that, contrary to the 'global' gene drive systems that would spread to all endemic regions, could be confined to a limited number of generations (temporally limited) and consequently limit the geographical spread of the technology (spatially limited). Thus, in 2016, Kevin Esvelt's MIT-based lab published a pre-print of an article detailing the successful proof of principle for a 'daisy-chain drive'.[67] Without delving too far into the molecular detail of the daisy-chain drives, they function by limiting the building blocks of biased inheritance within the population. Only those organisms with the full complement of building blocks can 'drive' the desired trait through the population. Over successive generations, the necessary molecular building blocks become less and less available before eventually none of the organisms within the population possess the full complement of building blocks and the gene drive 'drops out' of the population over time. As such, Esvelt's lab was said to have developed a gene drive with 'brakes'.[68]

From a safety perspective there are obvious reasons to prefer gene drives like the daisy-chain drive system. Both the spatial and temporal limitations of the daisy-chain system go some way in quelling fears about gene drive systems crossing across political boundaries and proliferating beyond their designers' control for better, or for worse. Whilst daisy-chain systems do not offer the 'off switch' we make use of in clinical trials, they do offer some promise of abating potential

[67] Charleston Noble, Jon Min, Jason Olejarz, Joanna Buchthal, Alejandro Chavez, Andrea J Smidler, Erica A De Benedicitis, George M Church, Martin A Nowak, Kevin M Esvelt, 'Daisy-chain Gene Drives for the Alteration of Local Populations' (2016) BioRxiv https://www.biorxiv.org/content/biorxiv/early/2016/06/06/057307.full.pdf Last accessed 15th June 2019. Now published in the Proceedings of the National Academy of Sciences, see: Noble *et al,* 'Daisy-chain Gene Drives for the Alteration of Local Populations' (2019) PNAS 116(17) 8275.

[68] Dustin M Graham, 'Putting the Brakes of CRISPR-Cas9 Gene Drive Systems' (2016) LabAnimal 47. The 'brake' analogy is a problematic one. The daisy-chain drives developed by Esvelt's lab cannot be 'turned off' at will, in the same way we might apply the brakes of our car at any time we like. Instead, the daisy-chain drives work in such a way as to drop out of the population after a certain number of pre-determined generations. If a daisy-chain gene drive was to cause harm following release it could still not be stopped or recalled prior to its predetermined endpoint. Thus it is more analogous to a car stopping because it has run out of fuel, than because the brakes have been applied.

harms. However, the development of daisy-chain drive systems undermines some of the virtues initially attributed to the new technology. In order to control vector populations over time, daisy-chain drives will require multiple, successive releases of gene drive organisms in much the same way that pesticides require regular re-application, bed nets need replacing and vaccines require re-administration. In turn, the economic benefits of technology are diminished and, furthermore, the technology presents itself as a commercially viable market product. Thus, the paradox: as gene drive technologies become less risky and safer, the potential benefits to host communities are reduced and the risks of commercialization increased.

It is the possibility that gene drive technologies become commercialised and therefore prohibitively expensive for the communities in which they were tested that raises exploitation-based concerns. In some ways, this argument is not particularly novel, but in others, it is. Many scholars suggest that clinical research trials carried out in developing countries where citizens will not be able to afford the drug tested within their borders once it reaches the market constitutes an exploitation of sorts.[69] Indeed, these claims lie behind the CIOMs Guidelines requirement for the 'reasonable availability' of the drug in the host country once it reaches market authorization.[70] However, Wertheimer resists such a claim. He argues that making a treatment available or unavailable within the host country following research does nothing to affect the truth conditions of an exploitation claim. As such the 'reasonable availability' requirement rests on a misunderstanding of exploitation.[71] This might be true – the benefit experienced by B during the trial is neither inflated nor diminished by the availability of the drug to his fellow citizens (let us call them C) once the trial is over. As the degree of benefit experienced by B is unaffected by the future availability of the drug to C, the fairness of the transaction between A and B is not altered. However, such claims in the context of gene drive research might miss the point. If B should have

[69] Ezekiel J Emanuel, D Wendler, J Killen, C Grady, 'What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research' (2004) Journal of Infectious Diseases 930.
[70] *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (CIOMS 2016).
[71] Wertheimer (n7) 209.

a need for the trialled drug beyond the research period, to deny them treatment when they cannot afford it once the trial is over makes the initial agreement between A and B unfair and therefore exploitative. As such, it is important to distinguish between obligations owed to citizens of host countries following research, and continuing obligations owed to research participants. In respect of the latter, Principle 30 of the Declaration of Helsinki states: "'[a]t the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic, and therapeutic methods identified by the study"[72] Thus, we can plainly say that in failing to provide the treatment or intervention for B once the research has concluded is unfair to B and therefore exploitative, whereas failing to ensure 'reasonable availability' to citizens of the host country is not.

In the context of gene drive research however, drawing a neat dividing line between those persons that we might consider 'research participants' (or, our class of Bs) on the one hand and 'future fellow citizens' (or, our class of Cs) on the other is not straightforward. Given the difficulties surrounding our ability to control and contain the spread of gene drive technologies, we cannot identify exhaustively those individuals whom the gene drive might affect during the research phase. Whilst the gene drive might be released in one area, it can and likely will spread to new areas and therefore new human populations. Put simply, we cannot straightforwardly distinguish between the class of Bs and the class of Cs. Therefore, we are almost always in the realm of having to ask whether the agreement between A and B is unfair when the treatment or intervention will be unavailable to B once the research has concluded. Above it was concluded with support from a range of scholars (Wertheimer included) and international agreements that such a state of affairs does constitute unfairness to B. Secondly, and again affecting the fairness of the agreement, in some instances the non-availability of the intervention following the trial period will make B's situation worse than it would have been had the intervention never been available at

[72] Declaration of Helsinki.

all.[73] In both of these cases, the benefit that B reaps in the transaction is diminished or even entirely negated, thus making the transaction unfair and the agreement between A and B exploitative.[74]

The claim here then, is that the commercialization of gene drive research might, in certain instances, render the research itself exploitative. Following Wertheimer, the truth conditions of an exploitation claim are met because we can demonstrate a benefit to A and an unfairness to B. A's benefit might manifest either in terms of the advancement 'personal and professional' interests discussed above, or the advancement of financial interests made possible by commercialization. Further, unfairness to B will manifest when B has been exposed to the risks that gene drive research carries and yet is deprived of any long-term benefit. In this case, we can describe the agreement between A and B ensuring B's engagement in the research as 'mutually advantageous exploitation'. The exploitation here is derived from the fact that B is not benefiting sufficiently, given the risks they are initially exposed too. In cases where B's situation might foreseeably be made worse by the withdrawal of gene drive once the research period has concluded, the exploitation that we have cause to worry about is no longer mutually advantageous, but harmful instead. In Section 4, I will suggest a range of strategic interventions that might be pursued in order to avoid either type of exploitation flowing from the commercialization of gene drive technologies.

3.2 Premature Field Release

The second instance in which I suggest that gene drive research might be exploitative, is those in which researchers push on toward open environmental releases of gene drives technologies before the range of risks have been properly identified and managed. Field releases might be said to be premature in one of two ways. In the first instance, a field release might be 'scientifically premature'

[73] Eradicating malaria for period of time before it then returns can be especially problematic as individuals can develop immunity to the plasmodium parasite that causes the disease. During periods in which malaria is suppressed, individuals not already bearing immunity will not develop it. As such, once the gene drive intervention has been halted and malaria returned to the region, individuals will be worse off for their lack of acquired immunity.

[74] Note, where the benefit to B is, in actual fact, negated we move from mutually advantageous exploitation to harmful exploitation.

– in these sorts of cases sufficient data has yet to be collected from contained use to make reliable predictions regarding risks and harms. The concerns about scientific prematurity of field releases described here reflect concerns identified in Bryan Wynne's account of uncertainty and ignorance.[75] That 'we don't know what we don't know' is a very real worry in the gene drive context. It has long been recognised that both research design and regulatory infrastructures fail to identify the aggregate threats posed by the interactions of multiple stressors and this concern is particularly acute in the ecological context.[76] Alternatively, we might say that a field release is 'socially premature' because it takes place in the context of inadequate infrastructures. Where this is the case, our concern is that host communities do not have access the relevant infrastructures should harm arise from the experimental release of gene drive technologies. One example might be the lack of access to adequate health care provision in cases where the use of gene drive technologies drives up rates of other vector borne disease. All the while, the research imperative pushes scientists toward overlooking these concerns in the pursuit of publishable findings.[77] The basic claim here in respect of both senses of prematurity is that early field releases expose B to unacceptable levels of risk, and it is those unacceptable levels of risk that make the agreement between A and B unfair, and therefore exploitative. Admittedly, there is a certain circularity in such a claim because in determining what constitutes unfairness (and therefore exploitation), we return to ask ourselves what the obligations of researchers actually are. However, we ought not shy away from the reflexivity of the problem, if in probing it, we are able to gain insight into how research ought to be designed in order to avoid the fears we identify. Further, if our aim is to gain an understanding of the wrongs that might be committed in gene drive research, it serves us better to start by asking whether an agreement is exploitative, rather than asking whether a researcher fails to fulfil their obligations. In the case of the exploitation question, whenever we identify

[75] Brian Wynne, 'Uncertainty and Environmental Learning' (1992) Global Environmental Change 112.
[76] For such a critic as applied to the European Union's chemicals regulation see: T Assmuth, M Hilden and M Craye, 'Beyond REACH: Roadblocks and shortcuts *en route* to Integrated Risk Assessment and Management of Chemicals' (2010) *Science of the Total Environment* 3954.
[77] Daniels (n9).

unfairness in the agreement, we have also identified a wrong in need of remedy, oftentimes before any harm is incurred. However, in the case of the obligation question, the wrong suffered by host communities can only be identified from an *ex poste* perspective and oftentimes only where the failure to fulfil the obligation has caused some or other harm within that community. As such, because we assess whether or not agreements are exploitative from an *ex ante* perspective, it is not necessary for any of the risks mentioned above to materialize in order for us to recognise a wrong committed against the human communities within which gene drive research happens.[78] Therefore, there are good practical reasons for considering premature field releases to constitute an instance of exploitation.

3.3 Gene Drive Research without Consent

Wertheimer is clear that, barring cases of what Feinberg calls 'harmless parasitism', where A derives benefit through his dealing with B and B does not consent, A exploits B in such a way as the moral force of the exploitation demands its legal prohibition.[79] As such, the consent of the human communities affected by gene drive research is a necessary pre-condition for non-exploitative research. In truth, the very discussion of exploitation in this chapter, which is by its nature an account of the fairness of transactions between parties, assumes some agreement or other between researchers and the human communities they interact with. However, when research is carried out in the absence of such an agreement (and, a fair one at that) the research is exploitative.

Defining precisely what we mean by 'consent' in this context is not an easy task. Quite plainly, there are lots of considerations in play here that do not plague already fraught conceptions of consent found within the mainstream medical law and bioethical literature. Whilst concerns about the epistemic position and voluntariness of potential participants are as keen here as in those other aforementioned contexts, additional complexity stems from the potential inability to exclude non-consenting individuals from trial design. For instance, is it the consent of individuals or

[78] Wertheimer (n7).
[79] Ibid.

communities that matters? Further, in what ways might societal structures or cultural factors impact on the way in which we answer that question? Therefore, questions remain around what sort of agreement constitutes 'informed consent' and what it means to withhold consent, which itself has implications for the sort of consent we consider sufficient to render the agreement non-exploitative.[80] These are complicated questions which this thesis alone cannot seek to answer, however, I do return to a further unpacking of issue in Section 5.

4. Avoiding Exploitation & Achieving Fairness

Section 3 strove to demonstrate the ways in which gene drive research might be exploitative and therefore how we might understand the wrongs suffered by human communities implicated in gene drive research. What was apparent in respect of all three concerns highlighted above (commercialization, prematurity and consent) was that, at present, we suffer from a deficient account of the obligations owed by researchers in this context. As such, this section seeks to do a number of things. In the first instance, it offers a way in, or a starting point, for thinking about what the obligations of researchers in respect of host communities might be. This is important because having such an account makes verifying the truth conditions of an exploitation claim more straightforward than might otherwise be the case. Thus, an understanding of researchers' obligations provides something of a normative standard against which we can assess the fairness of the agreement in question. Secondly, an account of researchers' obligations goes someway to prescribing the conditions that strategic interventions might impose to remedy the unfairness. Put simply, understanding what we think the obligations of researchers ought to be provides us with the means of preventing exploitation in the first place. Once an account of researchers' obligations has been offered, I move on to suggest the ways in which this account might avoid exploitation of the sorts described above. In this connection then, some time is devoted to thinking about the

[80] I say this because an account of what we do when individuals within a community withhold their consent offers some reflection on the purpose we think consent ought to be serving in those contexts. If gene drive research is pursued in communities where significant numbers of individuals or even a majority withhold consent, we ought to ask ourselves what ethical legwork consent is actually doing in this context.

sorts of strategic interventions that might be pursued in order to achieve fairness in gene drive research.

4.1 An Account of Obligations - Gene Drive Research as Human Subject Research

At present, an understanding of the obligations of researchers is obscured by the research community's description of those communities they interact with. This ambiguous understanding of the relationship between researchers and human communities therefore instantiates a paradigm of 'researcher paternalism' within which researchers decide their own obligations.[81]

It is notable that within the existing literature concerning the development and deployment of gene drive technology, the individual members of communities within which experimental releases will take place are not considered research participants or subjects. The National Academies Report, *Gene Drives on the Horizon*, uses the language of 'communities' and 'stakeholders', not participants or subjects.[82] Similarly, the report published jointly by the African Union and NEPAD refers only to 'stakeholders' within affected communities.[83] Furthermore, Target Malaria, the not-for-profit research consortium at the vanguard of research and development of gene drive technologies describes its own research protocols as placing importance on, and building toward, 'stakeholder engagement'. In its response to *Gene Drives on the Horizon*, Target Malaria describes the means by which they seek to record the 'opinions' of 'stakeholders' in respect of the research they are carrying out, as well as their future research plans.[84] However, describing members of affected populations as 'stakeholders' does not accurately describe either the practical or ethical quality of the research that is being carried out. Nor does the term adequately reflect the burdens to which communities might be subject during the research

[81] Emanuel and Grady (n5).
[82] Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct, 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' (Washington: National Academies Press) 131-146.
[83] Report of the High-Level African Union Panel on Emerging Technologies (APET), 'Gene Drives for Malaria Control and Elimination in Africa' http://www.nepad.org/publication/gene-drives-malaria-control-and-elimination-africa Last accessed 20th August 2019.
[84] Target Malaria, Response to the NAS Recommendations in: 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty and Aligning Research with Public Values' https://targetmalaria.org/wp-content/uploads/pdf/target-malaria-response-to-NAS-recommendations.pdf Last accessed 22nd May 2019.

process. Thus, I argue that when thinking about the experimental release of gene drive organisms there ought to be a presumption that human communities living in affected areas are human research subjects.

Whilst research into the efficacy of gene drive technologies does not naturally lend itself to inclusion under the banner of clinical research, recognising it as instance of human subject research ought to be an uncontroversial claim. The constraints placed on research and the centrality of the research subject within deliberations regarding the acceptability and/or legitimacy of any research activities both seek to achieve higher protections as regard to the safety and welfare of those individuals subject to research. Thus, the animating spirit of human research regulations are entirely congruent with the aims here.

Prior to the development of the international guidelines and regulations on human subject research discussed below, a paradigm of researcher paternalism prescribed the obligations of researchers in respect of the safety and wellbeing of research participants.[85] In the absence of prescribed ethical standards prevailed a research environment in which researchers decided the acceptability and legitimacy of their own practices and in which participant protection was a matter of researcher conscience. During this period, an 'unashamedly utilitarian' ethic dominated both the research agenda and research design, with little attention paid to the wishes, interests or needs of individual research subjects.[86] As such, the various international and domestic standards and agreements drawn up after a range of research atrocities, including Nazi experimentation, aimed at providing protections that the paradigm of researcher paternalism had failed to guarantee. In short, these instruments aimed to ensure respect for, and the safety of, research participants by prescribing the obligations of researchers. Further, in addition to seeking the proper protection of

[85] For a thorough account of the 'researcher paternalism' paradigm see: Ezekiel J Emmanuel & Christine Grady, 'Four Paradigms of Clinical Research and Research Oversight' (2007) Cambridge Quarterly of Healthcare Ethics 82.
[86] David J Rothman, 'Ethics and human experimentation—Henry Beecher revisited' (1987) New England Journal of Medicine 1195–9.

individual human research subjects, these guidelines articulated and demanded compliance with societally agreed values.

I argue that placing gene drive research beyond the scope of 'human subject research', and thus beyond the concomitant guidelines and regulations, situates its governance squarely within the researcher paternalism paradigm reminiscent of the pre-Nuremberg Code era. The researcher paternalism paradigm provides a deficient understanding of the ethical and legal obligations owed by researchers to the communities within which they test the technologies. As such, the claim here is that placing gene drive research within the ambit of the various international agreements governing human subject research is a necessary first step in increasing the oversight of gene drive research and, in turn, avoids exploitation and increases the safety of trial releases affecting both individuals and target communities. The next section examines gene drive research in light of the various international agreements regarding human subject research and makes the argument for its inclusion within this category of 'knowledge production'.[87]

4.1.1 Regulatory Definitions: 'Research' and 'Human Subjects'

The most obvious objection to describing gene drive research as an instance of human subject research is this: it is something qualitatively different to the sorts of research we have reason to think about in that context. For instance, gene drive research quite straightforwardly sits outside of the ambit of clinical research trials – the most common research activity in the human subject research context. Gene drive research does not necessarily entail the violations of bodily integrity characteristic of new drug trials and furthermore, individuals residing within the locality of a release site are not required to 'actively participate' in the study. Moreover, the parties to gene drive research do not occupy a doctor/patient relationship – a hallmark that plays a significant role in determining the obligations of the doctor-cum-researcher. Instead, the relevant relationship is one of investigator or researcher and participant where there exists a very real possibility that the

[87] Michelle N Meyer, 'Regulating the Production of Knowledge: Research Risk-Benefit Analysis and the Heterogeneity Problem' (2013) Administrative Law Review 237.

researchers responsible for an experimental gene drive will never come into contact with the members of the community into which they release the modified organisms. As such, researchers in the gene drive context are not bound by the obligations owed by doctors to their patients. For instance, the obligations owed to participants in human subject research under the Declaration of Helsinki appear to attach only to physicians and thus fail to implicate gene drive research.[88] In part, this is a consequence of the contested boundary between what constitutes 'research' and what constitutes 'the practice of medicine'.[89] Whilst some argue that the distinction between 'health research' and 'the practice of medicine' is that for the practice of medicine, the intervention is pursued for the sole purpose of improving the well-being of the individual patient.[90]

Others suggest that the difference between research and the practice of medicine lies in the intention of the researcher/physician.[91] Although that distinction is problematic in a number of ways, it is not too far from the distinction provided in the Belmont Report.[92] However, exactly where the border between research and medicine lies need not impede our understanding of gene drive research as an instance of human subject research, precisely because the clinical trial paradigm is only one example of the activities recognised as falling within the range of human subject research. Put differently, determining the extent to which gene drive research is, or is not, an approximation of clinical research offers an impoverished methodology, because considering clinical research as the archetypal instantiation of human subject research offers an overly narrow understanding of the range of research activities already falling within the domain of human subject

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[88] Declaration of Helsinki.
[89] Robert J Levine, *Ethics and Regulation of Clinical Research* (New Haven, Conn.: Yale University Press, 2nd ed1 988)
[90] The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research, 'The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research' (Washington, DC: Department of Health, Education and Welfare; DHEW Publication OS 78– 0012 1978).
[91] James G Hodge, 'An Enhanced Approach to Distinguishing Public Health Practice and Human Subjects Research' (2005) The Journal of Law, Medicine & Ethics 125.
[92] J W Buehler and S Burris argue that the CDC guidance on human subject research essentially draws up this intention-based distinction between research and the practice of medicine. See: J W Buehler and S Burris, *Research on the Impact of Law on Public Health.* However, and as James Hodge, amongst others, has pointed out, this intention based distinction is problematic, because two scenarios, each exactly the same, would be categorised differentially as either medicine or research, depending on the mental state of the researcher/physician. See: James G Hodge Jr, 'An Enhanced Approach to Distinguishing Public Health Practice and Human Subject Research' (2005) The Journal of Law, Medicine and Ethics 125, 128.

research. Furthermore, such a move fails to recognise the normative concerns reflected by the regulations imposed on any research involving human participants.

4.1.1.1 CIOMS Guidelines

In response to concerns about research being carried out in developing countries in order to save money and avoid the more restrictive regulations imposed by more economically developed States, the Council for International Organizations for Medical Sciences published a set of ethical guidelines. These guidelines, known as the *International Ethical Guidelines for Biomedical Research Involving Human Subjects,* describe human subject research as:

> activities designed to develop or contribute to generalizable health knowledge within the realm of research with humans, such as observational research, clinical trials, biobanking and epidemiological studies. Generalizable health knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based related to health, which can be corroborated by accepted scientific methods of observation and inference.[93]

In this way, given that gene drive research does indeed constitute an activity aimed at increasing generalizable health knowledge, and further, that research design will necessarily make use of observational and epidemiological study, on the CIOMS definition it can quite straightforwardly be described as an instance of human subject research.

4.1.1.2 US Regulations

Moving from international guidelines to national regulations, in the United States, the US Federal Regulations on research (more often known as the 'Common Rule') defines human subjects as:

> a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.[94]

'Intervention' is then further defined as both physical procedures (such as biopsies, venepuncture or the administration of pharmaceuticals) from which data is gathered, as well as manipulations of the subject's environment that are performed for research purposes. That these national regulations explicitly elucidate the range of research activities falling within the scope of human subject research is significant as it expressly includes interventions such as the release of gene drive

[93] International Ethical Guidelines for Biomedical Research Involving Human Subjects (CIOMS 2016) Preamble, xii.
[94] Federal Policy for the Protection of Human Subjects ('Common Rule'), 45 CFR 46.102 (f).

technologies. Furthermore, the notion that deliberate alterations of human environments might constitute human research is borne out beyond the Regulations. The controversy surrounding the Kennedy Krieger Institute Lead Paint Study of the 1990s is a pertinent example of how these issues play themselves out in practice.[95] In that study, researchers tested various lead abatement techniques, treating properties previously decorated with lead-based paint with various different reduction measures. The extent to which these various environmental methods were successful in reducing the lead content of the properties treated, in turn affected the health of the children residing within them. In this way, it is clear that researchers conducting trials with health-affecting consequences will find themselves subject to the regulatory apparatus governing human subject research, whether or not the research design implicates a 'doctor/patient relationship' or traditional understandings of what constitutes 'human subject research'.

Given the analysis above, I suggest that considering gene drive research an instance of human subject research is entirely consistent with existing regulatory frameworks surrounding biomedical research as a matter of both descriptive and normative fidelity. Further, and as already argued, having some account of researchers' obligations enables the identification and prevention of exploitative research practices.

4.2 Making Research Fair and Avoiding Exploitation

Having identified a general account of researchers' obligations to human communities and taking as our starting point the general obligations owed in the context of human participant research, I now turn to identifying some more specific obligations. Recall that Wertheimer suggests that in the case of mutually advantageous exploitation, we might pursue strategic interventions that seek to prescribe the 'acceptable terms of the transaction' in order to prevent exploitation. Below, I consider what might constitute 'acceptable terms' in the context of the sources of exploitation described in Section Three.

[95] David R Buchanan and Franklin G Miller, 'Justice and Fairness in the Kennedy Krieger Institute Lead Paint Study: The Ethic of Public Health Research on Less Expensive, Less Effective Interventions' (2006) American Journal of Public Health 781.

4.2.1 Long Term Availability of the Technology

Where gene drive technologies run the risk of becoming commercialized after a successful research phase, there exist legitimate exploitation-based concerns owing to the reduced availability of the technology. As such, I argue that the long-term availability of gene drive technologies for host communities (where the research has proven successful) is an essential condition for achieving fairness and avoiding exploitation. In one sense, this argument goes little further than the CIOMs guidelines requirement for 'reasonable availability' mentioned above. However, in reality, the imposition of such a condition is far more burdensome in the gene drive context than is the case with drug therapies or other health interventions.

Oftentimes, ensuring the reasonable availability of drugs or other health interventions can be achieved through certain intellectual property arrangements and/or market interventions.[96] In the contrast, the reality of ensuring that gene drive technologies are in the long term available to the communities within which they were once tested requires significant capital investment. If as seems likely, the gene drives which ultimately see release are of the 'daisy-chain' variety (as opposed to the single use 'global' gene drive systems) the sustainable use of gene drive technologies will require the development of significant technical infrastructures. This includes, but is not limited to, the building of insectariums, secure laboratories, and the education and training of scientists and laboratory personnel. Therefore, ensuring the continued availability of gene drive technologies extends far beyond making a drug product logistically and financially available. Significant capital investment of the sort required to ensure the long-term availability of gene drive technologies is clearly burdensome for researchers and their sponsors. so much so that it might in fact be considered prohibitively expensive. However, we ought to remain open to the possibility that in specifying the terms of a fair transaction between A and B, we end up, in all practical senses, prohibiting the agreement all together.

[96] For instance, consider patent exemptions under the TRIPs agreement. See: World Trade Organisation, 'WTO Members Agree to Extend Drug Patent Exemption for Poorest Members.' (2017) https://www.wto.org/english/news_e/news15_e/trip_06nov15_e.htm Last accessed 15th June.

Further, we might ask ourselves whether responsibility for ensuring the future availability of gene drive technologies ought to fall squarely and solely at the feet of researchers. Surely, it could be argued, governments of those states where the technologies are being deployed owe some assistance? Governments bear certain minimum responsibilities for the health of their citizens and will themselves benefit economically from the eradication of malaria.[97] Therefore, should state governments not also invest in the future availability of gene drive technologies? Much of the existing literature that concerns a critique of the CIOMs 'reasonable availability' requirement notes the practical difficulties associated with identifying who ought to bear the financial burden of making research findings available.[98] However, identifying all of those actors who might be said to owe financial investment in the long-term availability of gene drive technologies and, further, quantifying what constitutes an adequate or fair contribution by each, is far beyond the scope of this thesis. In many senses, it does not matter precisely who bears the cost of ensuring the long-term availability of gene drive technologies, as long as those costs are borne by someone. What we might require of researchers, instead, is that they provide a well evidenced plan and commitment, outlining how the long-term availability of the technology within trial regions will be funded. Only when we can secure the long-term availability of gene drive technologies for the communities within which the technologies were initially tested, can we say that the agreement between A and B (or in our case, researchers and host communities) are sufficiently fair as to be non-exploitative.

4.2.2 Interdisciplinary Research Design & Worst-Case Scenario Planning

The long-term availability of gene drive technologies described above is concerned with ensuring continuing and therefore adequate benefit to B in order to achieve fairness within the agreement between A and B. In contrast, requiring strongly interdisciplinary research is concerned instead

[97] Some estimates suggest that States within the African Union might together save up to twelve billion dollars annually if gene drive technologies can successfully eliminate malaria. For such an estimate, see: Outreach Network for Gene Drive Research, 'What is Gene Drive?' https://genedrivenetwork.org/#what-is-gene-drive Last Accessed 20th August 2019.

[98] Ezekiel J Emanuel, 'Benefits to Host Countries' in Ezekiel J Emanuel, Christine Grady and Robert A Crouch (eds) *The Oxford Textbook of Clinical Research Ethics* (Oxford: Oxford University Press 2008).

with reducing the risks to which host communities are exposed during gene drive research. Thus, whilst 4.2.2 focuses on achieving a sufficiently significant benefit in order to render the agreement between A and B fair, our concern here is ensuring fairness in the agreement between A and B by reducing the burden borne by B.

Requiring interdisciplinary research design reduces risks of harm, and therefore the burdens B faces, in a range of ways. Ensuring a sufficiently robust multi-disciplinary approach in research prior to field release avoids concerns regarding the 'scientific prematurity' described above. For many reasons, gene drive technologies are quite unlike any other technologies developed thus far. The range of risks they create and the values that they implicate are not the concern of one sovereign discipline. Gathering the data necessary to help determine their safety will require both creativity and imagination. The insight of mathematical biologists, ecologists, ethicists, anthropologists, epidemiologists, physicians, regulators, behavioural economists and lawyers will be required in order to develop an understanding of the multivalent threats. Failing to take interdisciplinary research design as a pre-condition of field release fails to pay due regard to the safety and well-being of host communities.

Much like the requirement for interdisciplinary research design, requiring investment in health and other infrastructures focuses on reducing the burdens and risks borne by the host community as a means of avoiding unfairness in the agreement between A and B. In section 3.1.2. we considered the 'social prematurity' of gene drive releases as a potential source of exploitation. I argue here that investment in, or the provision of, health and other infrastructures is essential to avoiding exploitation in gene drive research. Where A cannot evidence preparedness for the potential adverse effects of gene drive technologies, the agreement between A and B ought to be considered exploitative and strategic interventions that prescribe such planning as a necessary condition of the agreement between A and B ought to be pursued.

5. Consent

This section charts a brief discussion of the questions that the possibility of exploitation in gene drive research raise about the necessity and sufficiency of consent of target agents. This section does not, and cannot, aim to make any prescriptions about the quality of consent that ought to be required for gene drive research – that question alone is likely a thesis in itself. Instead, this section articulates some of the questions that any serious attempt at resolving this difficult issue ought to ask. As such, these are questions that lawyers attempting to build robust frames for understanding gene drive technologies must ask.

Before we begin however, a little is worth saying about what we understand about consent more generally. In law,[99] in ethics[100] and philosophy[101] there is broad agreement that consent worth having has two features. The first, relates to the informational condition of the agent giving assent to the proposed course of action. Whilst disagreement might exist about what precisely constitutes 'enough' information in order that the agent's consent is said to be valid, all agree that some information or other needs to be provided and that this information is understood. Secondly, most agree that the decision to give consent ought to be sufficiently voluntary, being free from coercion or undue influence. Disagreement exists regarding what constitutes coercion capable of defeating the giving of valid consent and, further, what other interferences might render the giving of consent insufficiently voluntary.

Disagreements about the intricacies aside, it suffices to say that in thinking about consent we have concern both for the information condition and the voluntariness condition of the target agent.

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[99] Alexander M Bickel, *The Morality of Consent* (Yale University Press 1977).
[100] Oonagh Corrigan et al, *The Limits of Consent* (Oxford University Press 2009); F G Miller and A Wertheimer (eds) *The Ethics of Consent: Theory and Practice* (New York: Oxford University Press 2010).
[101] Heidi Hurd, 'The Moral Magic of Consent' (1996) Legal Theory 121; Benjamin Freedman, 'A Moral Theory of Informed Consent' (1975) The Hastings Center Report 32.

5.1 Consent & Background Injustices

In order to understand what constitutes consent adequate to avoid charges of exploitation, a proper understanding of the relationship between consent and background injustices must be acquired. This itself entails asking several tricky questions. For instance, to what extent does the existence of background injustices affect the quality of consent? Do background injustices alter or affect the informational environment of agents to such an extent that the attainment of what is often known as the 'information' condition is difficult to attain? For instance, does a lack of education pose challenges to understanding the information delivered? Further, do background injustices affect the voluntariness condition so much so that it is hard to consider the agents consent to be freely given? In respect of the last question, the long shadow cast by legacies of empire and colonialism are hard to ignore.[102] All of the countries in which gene drive releases are currently planned are former colonies, as are all endemics regions in Africa, with the exception of Ethiopia. Moreover, the basic research informing the development of gene drive technologies, and the research teams delivering it, hail from former colonial powers.

Once these complex questions have been answered, we then have to ascertain what relationship, if any exists between the researchers, funders and regulators (or, 'source agents') involved in the development of gene drive technologies and the background injustices that we have identified. For instance, to what extent, if any, can the source agents be said to be responsible for background injustices that pose challenges to the quality of consent. Further, regardless of whether any causal relationship exists between source agents and background injustices, are there, nonetheless, duties of repair in respect of those background injustices held by source agents? Only once these questions have been answered can we diagnose instances of exploitation with any confidence.

[102] Jon Willis and Mark Saunders, 'Research in a Post-colonial World: The Example of Australian Aborigines' in Marian Pitts and Anthony Smith (eds) *Researching the Margins: Strategies for Ethical and Rigorous Research with Marginalised Communities* (Palgrave MacMillan 2007).

5.2 Whose Consent?

Once the questions above have been answered, there exists a second set of equally complex questions regarding *whose* consent it is that we ought to be seeking. Furthermore, we might consider the possibility that the quality of consent that we require varies across a range of target agents.

5.2.1 Individuals or Community Leaders – Cultural Question

Lawrence Gostin has recognised the pitfalls of applying highly individualised, Western models of consent to communities hailing from a range of different and varied cultures.[103] Furthermore, others have noted the risk of ethical imperialism, or the risk of 'the imposition on one society of solutions culturally appropriate to another society, on the pretext that they represent ethical absolutes'.[104] In this regard then, we must be aware that those whose consent is required in order to defeat claims of exploitation might not in fact be individually affected agents, but community leaders or representatives instead. As Christakis notes, the very concept of 'respect for persons' that systems of informed consent are designed to protect are at odds with '…more relational definitions of the person found in other societies, which stress the embeddedness of the individual within society and define a person by his or her relations to others'.[105]

In this way there might be some disconnect between those persons that we identify as individually affected target agents, and those from whom we seek consent or permission for the commencement of gene drive technology research.

5.2.2 Target Communities or Neighbours – Spatio-Political Questions

Secondly, there are spatio-political questions that arise with regard to whose consent it is that we think matters. Do we require the consent of target agents residing within the immediate locality of a proposed release of gene drive technologies? Or, instead, do we require both their consent and that of their closest neighbours? Recalling the water fluoridation example discussed in Chapter

[103] Lawrence Gostin, 'Ethical Principles for the Conduct of Human Subject Research: Population-Based Research and Ethics' (1991) Law, Medicine and Healthcare 191.
[104] F Gilks and J B O Were, 'Ethical Imperialism' (1990) New England Journal of Medicine 322.
[105] N A Christakis, 'The Ethical Design of an AIDs Vaccine Trials in Africa' (1988) Hasting Center Reports 31.

Four, do we require the consent of political or administrative neighbours too? Furthermore, if we think that the consent of all the above listed parties is required, do we expect the same quality of consent to be rendered by all? Is it the case that whilst there might be a high threshold for what constitutes sufficient consent from those agents living within the immediate locality of a proposed release site, something lesser is required of neighbouring agents?

It is also important to reflect on the way in which questions about consent play a significant role in framing the way that we think about gene drive technologies. Understanding whose consent it is that we think is relevant tells us something about the target agents that we include within the frame that we build for gene drive technologies.

6. Conclusion

This Chapter has sought to argue that when we are thinking about the wrongs, harms or overflows that the use of gene drive technologies might generate, questions surrounding the possibility of exploitation should be squarely within the frame.

To summarize, albeit briefly: the benefits of including questions of exploitation within the frame are manifold. Paying attention to the fairness of the way we transact with target agents has the potential to improve the safety of deployment by focusing attention on a range of questions that would likely otherwise go unasked.

Moreover, understanding how fairness might be achieved requires us to build a frame that looks both forward and backwards. Backwards, because understanding the social and political histories of target communities is relevant to understanding what constitutes fairness in any given circumstance. Forwards, because the continued use, availability and effects of these technologies past the research stage bear implications for fairness too in the ways that redistribute both benefits and burdens. Furthermore, bringing to the table all of the information required to make assessments of what fairness demands, is by its nature an interdisciplinary approach – the insights of ethicists, historians, anthropologists and economists can all be relevant to understanding what constitutes fairness, or a fair transaction in the circumstance at hand.

As such, imbuing the framing process with concern for ethical questions, and with an eye on exploitation in particular, ensures that the understanding of gene drive technology that we ultimately arrive at is bounded by a sufficiently broad frame.

CHAPTER EIGHT: CONCLUSION

As warned, we arrive at the last Chapter of this thesis with no ready-to-go roadmap for the regulation of gene drive technologies in sight. However, much has been achieved. The path to the safe and effective regulation of gene drive technologies that the reader might well demand is much straighter, and far shorter than it was when they opened those first pages. Much of my effort in the preceding Chapters has been directed at driving the reader off the beaten track and, in doing so, showing them that there is so much more to be considered when thinking about the regulation of gene drive technologies than the view from the highway reveals. Before I go on to draw out the conclusion that we arrive at, I take some time now to review the progress that has been made so far.

This thesis has demonstrated that when we as lawyers go about the business of describing new technologies as regulatory objects (gene drive technologies being no exception) we build frames to understand them. In building those frames, we attach varying degrees of significance and importance to different aspects and features of the technology. We sift through the information that we have about them and decide which features of the technology are relevant for the purposes of regulation and which are not. In building these frames we make judgements about the overflows that regulation should seek to contain or avoid, the persons that the regulation should seek to protect or empower and the persons or organizations that the regulation ought to hold responsible for ensuring good outcomes.

However, the overflows, target agents and source agents that we consider relevant can only be divined from the information and values through which we have sifted. On occasion, the knowledge claims represented in the information we sift through fail to represent the totality of what we ought to know when we go about constructing our frames. As such, at times, the frames we build fail to bear fidelity to the technologies as they exist in reality, and the implications that they might have for the ways in which we go about living in the world.

It is not, however, all doom and gloom and ill-fitting frames. Given the idiom of co-production as described by Sheila Jasanoff – the understanding that both science and social orders are mutually constituted – lawyers need not give in to the mores of technological determinism in how they build frames and describe new technologies as regulatory objects.[1] Instead, lawyers have a very real choice about the ways in which they go about framing and the knowledge claims and expertise they take into account when seeking to render a description of new technologies as regulatory objects.

In Chapters Two and Four, I demonstrated that, for the most part, understandings of gene drive technologies as regulatory objects have been arrived at taking account of technical expertise almost exclusively. Chapters Three, Six and Seven showed the reader that in describing gene drive technologies as regulatory objects, there is so much more to think about than can be captured or articulated by technical expertise alone. Much of the heavy lifting in the preceding Chapters has consisted of putting the complexity of gene drive technologies on screen and highlighting the implications of failing to do so. The challenge there has been bringing together analysis informed by a range of domains, all with slightly differing concerns – law, regulation, ethics, anthropology and beyond. Only in light of all of these analyses can the challenge, complexity and overflows associated with gene drive technologies be fully understood.

In the first instance, framing gene drive technologies by reference to technical expertise alone has the effect of describing them as regulatory objects amenable to regulation by pre-existing regulatory regimes. Chapter Four demonstrated that present thinking around the regulation of gene drive technologies characterises it as a technology adequately regulated by existing frameworks governing the development and releases of GMOs. By way of example, I considered the suitability of the European Union framework for regulating GMOs as a means of regulating gene drive technologies. That analysis demonstrated that, for a range of reasons, the EU GMO

[1] Sheila Jasanoff, 'The Idiom of Co-Production' in Sheila Jasanoff (ed) *States of Knowledge: The Co-Production of Science and the Social Order* (Routledge 2004).

framework cannot control or avoid the various overflows generated by gene drive technologies, nor can it protect the populations of target agents affected by their release. Gene drive technologies present a range of challenges – social, cultural, political and ethical that are absent in the GMO context and therefore generates regulatory disconnection.

Once the flaws of overly narrow, technical frames had been drawn out, Chapter Five moved on to demonstrate a series of framing triumphs in law. Taking public health law as an example, I demonstrated that lawyers can and have built frames capable of aptly capturing the complexity of the problems or technologies that they are tasked with regulating. The two examples put forward – the legislation of the sanitary movement and the water fluoridation legislation – demonstrated the ways in which lawyers have mandated a range of knowledge claims be scrutinized in making decisions. The water fluoridation legislation in particular provided an illustration of just how broad frames of understanding might be. Section Six of the Water Fluoridation regulation requires scientific evidence to be scrutinized, reviewed and regularly updated.[2] Further, decision makers have to take account of public opinion as well as the state of local infrastructure and its ability to bear the additional burden that fluoridating water supplies might apply and the economic effects of deciding to fluoridate or not. Thus, in building frames for understanding the implications of fluoridating shared water supplies, lawyers have understood and acted upon the importance of making decisions on the basis of a range of knowledge claims, and in mandating the regular updating of scientific understandings of the effects of fluoridation have made prescriptions in respects of how research ought to be conducted and stipulated the range of questions scientific findings ought to answer.

Building on the example provided by public health law, Chapters Six and Seven demonstrated the ways in which substantive ethical enquiry might render thicker descriptions of the implications of deploying novel or emerging technologies. In this way, these ethical

[2] The Water Fluoridation (Proposals and Consultation) (England)Regulations 2013, s 6.

explorations helped to develop frames more faithful to the realities of the technologies under consideration, expanding our understanding of these technologies as regulatory objects. For example, the discussion of relational approaches to questions regarding the moral status of species in Chapter Six demonstrated the if we are to fully understand the range of possible overflows, technical experts must answer a range of questions about social behaviours of the species in question. Further, the analysis of the ethics of exploitation in Chapter Seven demonstrated why gene drive research ought to be considered an instance of human subject research for the purposes of regulation.

This thesis offers two sets of conclusions. In the first instance, we can reach some conclusions as to how we ought to go about regulating gene drive technologies specifically. However, from the analysis pursued in the preceding pages we might also draw some conclusions about how lawyers ought to go about describing new technologies as regulatory objects more generally. These two sets of conclusions are presented in turn below.

1. Thinking About Regulating Gene Drives Technologies

The first, and perhaps most obvious conclusion that we can draw with respect to gene drive technologies is that *not regulating* is not an option. The risks associated with gene drive technologies, and the overflows that it might generate are without precedent. The European Union GMO regime that some have put forward for the regulation of gene drive technologies is, as was demonstrated in Chapter Four, radically inadequate. Any attempts to regulate gene drive technologies as a GMO will generate an instance of Brownswordian regulatory disconnection, with real implications for the human communities affected.[3]

In the face of regulatory disconnection there are two options – hope that careful judicial innovations and/or a range of statutory tweaks might bring about reconnection or return to the drawing board entirely. In order to achieve reconnection for gene drive technologies there is no

[3] Roger Brownsword, *Rights, Regulation and the Technological Revolution* (Oxford University Press 2008) 160-184.

choice but to return to the drawing board and draft anew. Fresh consideration of the range of overflows that gene drive technologies might generate is required, if we are to draw up a frame that bears fidelity to the technology as a regulatory object. Having placed all of the complexities and overflows generated by gene drive technologies on screen, and given that existing regulation is inadequate and not regulating at all is not an option, I suggest that a *sui generis* framework ought to be developed. Notably, and perhaps most importantly, only through the exploration of ethical enquiry and through the application of non-technical expertise is it possible to arrive at such a conclusion.

1.1 A Licensing Framework for Gene Drive Technology Research

I have, throughout this thesis, avoided making absolute prescriptions with regard to how gene drive technologies ought to be regulated. However, this section might be thought of as one exception. Drawing on all that has gone before, I suggest that gene drive technologies ought to be regulated through an *ex ante* licensing framework. As such, I am advocating for a command and control model of regulation for gene drive technologies.[4] Licence-based models of regulation are not unusual when it comes to the regulation of risky activities, and this section discusses the reasons for which this approach ought to be favoured in the context of gene drive technologies.[5]

As became apparent throughout Chapters Six and Seven, it is not possible to take just one universal position, ethical or otherwise on the use of gene drive technologies. It is not possible, or even desirable to say that all gene drives, for all purposes, in all places ought to be impermissible. Instead, the permissibility of any given deployment of gene drive technologies depends on a variety of factors, and thus consideration ought to be made on a case by case basis. Requiring researchers intending to develop gene drive systems in the laboratory for eventual environmental release to obtain a license allows for scrutiny on a case-by-case basis.

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[4] Robert Baldwin, Martin Lodge and Martin Cave, *Understanding Regulation: Theory, Strategy and Practice* (Oxford University Press, 2nd Edition 2012) 106-111.

[5] Terence Daintith, 'The Techniques of Government' in J Jowell and D Oliver (eds) *The Changing Constitution* (Oxford: Clarendon Press, 3rd Edn 1994) 209-236.

As a mode of regulation, requiring individuals or organisations to obtain a license has several benefits with regard to risk activities *per se*. That is, there are some benefits that accrue, not contingent on the nature of the technology that we are seeking to regulate. The most obvious, is that a licensing framework articulates a clear position *viz a viz* the ordinary permissibility of the activity in question. That is, without a license research is unlawful and thus: no license, no research. This position is quite apart from the current situation for gene drive technologies, where, in the absence of any articulated regulatory position, research continues on, regardless of the concerns that might exist. Furthermore, and with respect to the Rule of Law considerations picked up throughout Chapter Four, all actors and potential actors are able to straightforwardly ascertain the lawfulness of their proposed research activity.

Secondly, requiring researchers to obtain a license allows regulators to draw up a register of all past and ongoing research. In this way, regulators are able to assess the overall picture of progress and advancement. For instance, are there more applications for licenses and more licenses granted for certain applications of the technology? Understanding what general trends in research progress might tell us about the future direction of travel presents the opportunity to make timely decisions about the desirability of likely future developments. In this way, the tendency of regulators to be outpaced by developments in the lab might be made less acute.

Thirdly, a licensing-based approach to the regulation of risky activities enables the regulator to place conditions on how research is pursued. Subjecting the granting of licenses to conditions is an important means by which certain overflows can be controlled or the interests of certain target agents be taken account of. Enabling regulators to exert direct control over the way in which science is conducted and technology developed plays a significant role in allowing for directionality in the mutual constitution of science and the social order.

However, a licensing model of regulation has particular benefits in respect of gene drive technologies specifically, not just the regulation of risk activities more generally. In the first instance, requiring researchers to obtain a license before any research might be taken up ensures

regulatory oversight from the earliest stages of technological progress. This in turn has the benefit of being able to shape the way that science is done and research pursued allowing for the possibility that the ethical enquiries pursued in the Chapters above might play a role in articulating the questions that technical expertise must answer, if we are to develop fuller understandings of gene drive technologies and their implications. As such, licensing conditions can play a role in embedding values at the earliest stage of the research enterprise, bringing ethical thinking into the purview of both regulators and scientists.

1.1.1 Establishing a Licensing Authority

A necessary consequence of advocating for a licensing-based model of regulation, is establishing a body with the authority to grant licences and enforcing the conditions that they prescribe. The transnational aspect of gene drive research makes questions surrounding the jurisdictional identity of such an authority particularly complex. Research happens in one state, but release takes place in another – so where should the regulator be located? Further, given the ability of the technology to move across political borders following release, international harmonization is desirable. As such, this has led some to suggest that an international regulator ought to be favoured over domestic, national regulators working in collaboration with one and other.[6] Elizabeth Fisher has noted the effect that the abstract concept of 'the state' has had in constraining academic imagination,[7] and it is striking that preference for an international regulator fills the gap within which we fail to recognise any alternate means by which collective decision-making across borders might be pursued. The most desirable solution for the regulation of gene drive technologies probably lies in internationally agreed regulations enforced by national regulators with responsibility for assembling the requisite expertise and making decisions in conjunction with national regulators in other affected states. In this respect, some insights might be drawn from the

[6] National Academies of Science, Engineering and Mathematics Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct, 'Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values' (Washington: National Academies Press).
[7] Elizabeth Fisher, *Risk Regulation and Administrative Constitutionalism* (Hart Publishing 2007) 11-12.

operation of the International Commission on Radiological Protection and its success in securing international harmonization and national implementation of recommendations pertaining to the safe use of ionising radiation.[8]

Whilst this section has argued that gene drive technologies ought to be regulated through a licensing-based system, that is perhaps as close to any concrete prescriptions as this thesis gets. Whilst the reader's appetite for a ready to go framework might have been whetted, the next section moves away from making any hard and fast recommendations. Instead the following section describes a range of issues that I suggest regulators ought to take account of when deciding whether or not to permit gene drive research, and where it is permitted, under what conditions.

2. Substantive Concerns for Regulating and Regulators

What precisely ought to be demanded of licensees and licensors cannot possibly be resolved here. Instead, this section focuses on two things. Firstly, the substantive issues that will have to be taken account of when developing a regulatory framework. Secondly, the substantive issues that regulators will have to take account of when deciding whether or not to grant a research license and, if so, what conditions that license ought to be subject to. Perhaps, more important than the content of the concerns themselves, is the understanding that, absent the ethical enquiries pursued in Chapters Six and Seven, consideration of these issues might never make it into our frames of understanding and therefore descriptions of gene drive technologies as a regulatory object. None of the concerns described below are accessible through the application of technical expertise alone.

2.1 Institutional Resources

Beyond the resources required in order to establish a statutory licensing body like the one described above, significant resources will also be required in order to ensure that it regulates effectively. For example, employing the wide range of expertise that this thesis has argued is crucial to the proper regulation of gene drive technologies will not be without significant cost. The

[8] R H Clarke and J Valentin, 'The History of the ICRP and the Evolution of its Policies' (2008) Annals of the ICRP 75.

expertise required for adequately informed regulatory decision making will include that of regulatory scientists, ethicists, social scientists, lawyers, clinicians, and those with particular cultural expertise too. Assembling panels of appropriately qualified and knowledgeable persons itself requires the investment of significant institutional resources. However, the existence of such panels is not without precedent. For example, the constitution of expertise with the Human Fertilization and Embryology Authority provides a promising example of a decision-making panel capable of scrutinizing a varied range of knowledge claims. At the time of writing, the HFEA benefits from the expertise of civil servants, management consultants, practicing lawyers, academic lawyers, ethicists, clinicians, research scientists, faith leaders, lay people and service users.[9]

Beyond the institutional resources required to identify and retain the broad range of expertise necessary for decision making, significant infrastructural investment will also be required. For example, devising and overseeing the long-term monitoring of gene drive technologies following deployment will require the development of significant technical infrastructures. In this way, it ought to be understood that the regulation of gene drive technologies will present a significant economic burden to those states seeking to regulate their use.

This is no great surprise – economic critiques of command and control-oriented regulation dominate the recent regulatory literature.[10] However, the implications of the economic burdens of command style regulation and its associated informational demands will vary from state to state. Given that all of the states within which scientists are proposing to release gene drive technologies in the not so distant future are designated as 'least developed countries' by the United Nations Committee for Development Policy, there are challenging questions about the range of feasible institutional designs for regulation.[11] In developing countries where institutional and infrastructural

[9] Human Fertilization and Embryology Authority, 'Meet Our Authority Members' https://www.hfea.gov.uk/about-us/our-people/meet-our-authority-members/ Last accessed 22nd September 2019.
[10] Anthony Ogus, *Regulation: Legal Form and Economic Theory* (Hart Publishing 2004) 337-340.
[11] --, 'List of Least Developed Countries (as of December 2012)' (United Nations of Committee on Development Policy) https://www.un.org/development/desa/dpad/wp-content/uploads/sites/45/publication/ldc_list.pdf Last accessed 22nd September 2019.

capacities are limited, the challenges associated with command style regulation such as a licensing model are particularly acute.

In the context of gene drive technologies, these economic, regulatory and infrastructural disparities present a particular challenge for regulatory design and the actualities of going about regulating. The activities that need to be regulated – research, experimental release and release – occur in different states with different economic realities, each with different implications for regulation. Whilst the basic, lab-based research takes place in developed countries with reasonably developed regulatory infrastructures and access to significant institutional resources, the experimental release of gene drive technologies is scheduled to take place in least economically developed state with limited regulatory infrastructures and little, if any, access to institutional resources.

Whilst perhaps the most obvious solution would be the establishment of an international regulator, equipped with all the necessary institutional resources and a peripatetic licensing task force, such a solution is not without significant drawbacks. As Baldwin, Cave and Lodge note, 'transnational companies dominate the regulatory process, international organizations produce imposed blueprints, and domestic elites shape international pressures in their own self-interests'.[12] If Baldwin, Cave and Lodge's diagnosis of the situation is correct, then pause is required. It might well be more desirable to appreciate the existence of these disparities and their implications, than to advocate for a single international regulator capable of insulating regulation from institutional and infrastructural deficiencies at the national state level. Instead, significant attention ought to be paid to improving regulatory capacity in the least economically developed states, rather than supplanting their regulatory function with an international regulator.

[12] Baldwin, Cave and Lodge (n4) 415.

2.2 Not-for-Profit Agenda

Chapter Seven highlighted the ways in which the commercialization of gene drive technologies might harm the communities within which they are initially tested or released. For instance, if commercialisation resulted in the withdrawal of gene drive technologies from a region within which they had previously been used due to their unaffordability, serious harms would be suffered by local communities. Beyond the tangible harms, the commercialization of gene drive technologies following experimental use within target communities might also constitute exploitation as described at length in Chapter Seven.

As such, in order to avoid both the bodily harms and ethical wrongs that might flow from the commercialization of gene drive technologies, regulators ought to pay considerable attention to the potential for commercialising any gene drive application under review. Further, where possible, the commercialization of these technologies ought to be prohibited. Where a prohibition on commercialization is not possible, regulators ought to ensure that the commercialization of the technology will not threaten its long-term availability within the populations within which it was released. As such, ensuring that commercial applications of gene drive technologies will not defeat the long-term availability of gene drive technologies for public health ought to be a key concern of any regulatory framework moving forward.

2.3 Rescue Infrastructures

Finally, regulators ought to consider the infrastructural conditions of the region within which release is proposed. The ability of the state in question to halt and reverse the harms occasioned by gene drive technologies ought to be central to the decision to grant or refuse a licence, or to determine what conditions might be imposed on the holding of a license. Chapter Two highlighted the ways in which discussions surrounding the possibility of halting and reversing harms caused by gene drive technologies have been limited to the proffering of technical solutions alone: for instance, developing 'reversal drives' in order to counter the errant genetic changes and prevent

them from spreading any further.[13] However, and as this thesis has contended throughout, regulation ought to not be limited to the contemplation of technical solutions alone.

As such, regulators ought to recognise that in order to answer questions about how harms flowing from gene drive technologies might be avoided, controlled or minimized, the availability of certain infrastructures is relevant. That being the case, there ought to be significant focus on the availability, accessibility and quality of healthcare in states considered for the experimental release of gene drive technologies. If a release of gene drive technology were to increase the rate of disease burden at the population level, or increase the severity or even lethality of the disease, it is the availability of healthcare and curative treatment, rather than the availability of a reversal drive, that is relevant to the avoidance and reduction of gene drive related harms. Furthermore, in a situation in which gene drive technologies fail to be effective after a long period of efficacy, it is the state's ability to quickly and effectively deploy more traditional vector control techniques that will determine the extent of the harm suffered by human populations.

A necessary part of moving beyond the hegemony of technical expertise in thinking about the regulation of gene drive technologies is taking account of the infrastructural conditions of the state within which they will be released. As such, I argue that a considerable part of the task for those making decisions about whether or not to grant a license entails understanding the availability of certain 'rescue' infrastructures or requiring significant investment as a condition of the license. As was discussed at some length in Chapter Seven, the availability or otherwise of these various different infrastructures will have a significant bearing on whether or not any given gene drive release might be considered exploitative.

[13] K Oye et al, 'Regulating Gene Drives' (2014) ScienceXpress 7658.

3. Thinking About Regulating Novel Technologies Generally

In addition to contributing to debates surrounding the regulation of gene drive technologies, this thesis offers a contribution to debates that focusses on how we ought to go about regulating novel technologies more generally.

When science and technology make unexpected leaps forward, it is quite natural that we as lawyers reach for pre-existing frames. It is far easier to think of the situations with which we are confronted as 'cold' and interests already identified and settled than it is to acknowledge that they are instead hot situations in flux.

The regulation of gene drive technologies presents no exception, with discussions identifying gene drive technology as an instance of a 'green biotechnology'. As noted in Chapter Four, prior debates surrounding the regulation of gene editing technologies spilt themselves into two distinct camps – the regulation of gene editing for human applications and the regulation of gene editing for non-human applications. This red/green biotechnology binary as a means of framing emerging biotechnologies has played a particularly powerful gatekeeping role when it comes to defining which knowledge claims are considered relevant and appropriate to regulatory decision making. Whilst, from their conception, the ethical implications of red biotechnologies have been recognised and debated at length in the regulatory arena, the regulation of green biotechnologies has, for the most part, been considered absent of value judgments or greater ethical implications. Instead, questions surrounding the use and proper regulation of green biotechnologies have (although not without considerable academic critique) been treated as resolvable by technical expertise and scientific findings.[14] As such, these frames have played a significant role in the way we have conceived of each of the technologies as regulatory objects, as well as in prescribing the range of expertise and knowledge claims taken account of in framing.

[14] For a critique of the dominance of technical expertise in respect of the regulation of green biotechnologies see: Maria Lee, *EU Regulation of GMOs: Law and Decision Making for a New Technology* (Edward Elgar 2007) 225.

However, by virtue of the expertise and knowledge claims they admit of and those that they exclude, the frames that we chose to borrow, and even those that that we build from scratch, can fail to bear fidelity to the realities of the technologies that we are trying to regulate. Ill-fitting frames can present a host of challenges, with regulatory disconnection perhaps the most challenging among them. Despite the enormity of the challenge posed by regulatory disconnection, the fact that existing frames fail to fit is often easily overlooked because it is not always obvious that the disconnection is generated by an ill-conceived frame. This is further compounded in contexts within which reliance on technical expertise dominates, as relying only on technical expertise will continue to affirm that, at least on the view of technical experts, the frame is fit for purpose.

The idea that in order to build better fitting frames, bearing greater fidelity to the phenomena they are designed to describe, a wide range of knowledge claims and expertise are required is nothing new. Much of the literature at the intersection of law, science, regulation and policy makes similar claims. However, in describing the problem as simply one of science versus value, as much of the literature does, there is a risk that we come to understand the issue in terms of a Science/Democracy dichotomy.[15] Either decision-making in areas of high technological complexity ought to be made primarily on the basis of technical expertise, or instead primarily on the basis of publicly determined values – for from where else might the values we require be derived? If we choose to conceive of the problem this way, the line that divides questions of science and questions of value is bright and its implications immutable. Either we believe regulatory decisions ought to be made through the application of scientific findings, or through the application of values prescribed by public opinion.

[15] For a discussion of this phenomena in the context of the regulation of technological risk see: Elizabeth Fisher, Risk Regulation and Administrative Constitutionalism (Hart Publishing 2007). For those on the science side, see: Examples include National Research Council, *Risk Assessment in the Federal Government: Managing the Process* (Washington DC, National Academy Press, 1983); J Graham, 'Making Sense of Risk' (2000) 20 *Risk Analysis* 302; and C Sunstein, *Risk and Reason: Safety, Law and the Environment* (Cambridge, Cambridge University Press, 2002). For those on the democracy side, see: D Fiorino, 'Environmental Risk and Democratic Process: A Critical Review' (1989) 14 *Columbia Law Review* 501; and R Kennedy, 'Risk, Democracy and the Environment' (2000) 20 *Risk Analysis* 306; Maria Lee, 'Beyond Safety? The Broadening Scope of Risk Regulation' (2009) Current Legal Problems 242.

As such, oftentimes, those championing the role of public participation do so in response to the same problem that I describe throughout this thesis – the idea that regulatory decision-making ought to rely on more than technical expertise if it is to correctly characterize and resolve the problems that it is charged with. However, it is in promulgating an apt solution to that problem that myself and those above part company. Those who conceive of the lack of wider expertise and value judgements in regulatory decision making as a symptom of a democratic deficit pose public participation as a solution. By embedding public participation in regulatory decision making, decision making is infused with a wider range of expertise and a vast range of values extending beyond the technical domain might be brought to the table.

However, I suggest that thinking that public participation is the only, or at least most desirable, means by which expertise might be extended beyond the technical and values assessed is a mistake. That is not to say that public participation does not widen the range of expertise and values brought to the decision makers' attention – it surely does, as it presents a whole range of knowledge claims and values that would not be taken account of otherwise. However, public participation does little to assist in determining which of the knowledge claims and expertise presented are relevant to the decision being made and what information we ought to demand. Instead, public participation provides an exercise of what in Chapter Four I called 'collective epistemic collation', rather than the collective epistemic responsibility that I am arguing for.

The reason that public participation fails to improve decision-making in any meaningful way, is because it offers a solution that flows from a very particular description of the problem it purports to solve. Public participation is presented as a solution to a problem generated by an objective and abiding divide between questions of science and questions of value, with no possibility of an interplay between the two. Put simply, public participation is a solution which fails to recognise the realities of co-production. In reality, the dividing line between science and democracy is neither bright nor immutable because both science and the social order are mutually constituted.

Once an understanding of the significance of co-production draws out the falsity of any supposed hermetic seal separating science and value, attempts to broaden the range of relevant expertise required for good decision making need not be confined to the bald importation of public opinion. Instead, and as I have argued throughout this thesis, substantive ethical enquiry and expertise can, and ought to, be embedded at the earliest stages of the regulatory process – in developing the frames through which we understand emerging technologies.

Quite unlike public participation, ethical enquiry can play a significant role in identifying the expertise and knowledge claims that are relevant to our understandings of new technologies as regulatory objects. By rendering thicker descriptions of the phenomena with which we are confronted, ethical enquiry places us on the road to bridging troublesome epistemic gaps, by articulating the questions that science and publics need to answer before our understandings of novel technologies and their implications can be considered sufficient to allow for regulatory decision making that bears fidelity to the realities of these emerging regulatory objects.

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