

Section 7

Other applications

Section 7 – Other applications

Overview

Genome editing has potential applications in a range of settings, including energy and industrial production, military and even leisure applications, in addition to those covered in previous sections. Many of these involve the manipulation of microorganisms and aspire to rational design approaches characteristic of the field of synthetic biology.

The relationship between genome editing and synthetic biology is discussed and the enthusiastic uptake and development of genome editing tools among synthetic biology practitioners is noted. The interdisciplinary approach of much synthetic biology research, which integrates social and ethical reflection, is contrasted with models in other areas of research.

The value of genome editing in developing the bioeconomy is discussed, as are areas in which genome editing may accelerate or facilitate industrial production using microorganisms. The ease of use of CRISPR-Cas9 alongside or outside institutional settings (in organised competitions, or for community or private research, or for artistic and cultural purposes) is discussed. A range of biosafety measures are noted and the question of the criteria according to which they should be engaged recurs.

Applications of genome editing of potential interest to the military are enumerated although the difficulty of researching this area is highlighted. A number of biotechnology-related initiatives in the UK and US defence communities are outlined and the implication of genome editing in these is noted. Biosecurity and potential dual use issues are noted, and differences in perspective between the security and scientific communities, and between the UK and US, are identified.

A number of moral and societal questions are identified, including the difficulty of applying conventional regulatory mechanisms based on institutional membership, market regulation, cost or knowledge barriers.

Introduction

- 7.1 Genome editing systems have applications across biology, including plants, animals and humans, but the most promising system currently, CRISPR-Cas9, is based on a viral defence mechanism endogenous to bacteria.⁴²⁹ Bacteria are ubiquitous and represent some of the simplest forms of cellular life.⁴³⁰ The bacterial biomass may well outweigh the combined mass of all plants and animals on earth.⁴³¹ Microorganisms, through which the rest of the biosphere is connected to the non-biological environment through uptake and conversion of energy and chemicals that support life, are fundamental to life on earth.⁴³² (For example, the community of bacteria in the gut – the gut microbiome – is necessary for digestion of food and its composition is increasingly linked to disease predisposition.⁴³³ The energy-generating organelles in eukaryotic cells, mitochondria, and the photosynthetic organelles of plants, chloroplasts, are thought to be derived from bacteria that were incorporated at an early phase of plant and animal evolution.⁴³⁴) The plasticity of microorganisms and their ability to adapt to environmental challenges through rapid genome evolution, makes them both useful as potential sources of chemical compounds but also potentially harmful (pathogenic).⁴³⁵
- 7.2 Genome editing is a potentially valuable tool in industrial biotechnology, further transforming manufacturing processes, generating new products, reducing pollution, improving resource

⁴²⁹ Doudna JA and Charpentier E (2014) The new frontier of genome engineering with CRISPR-Cas9 *Science* **346**(6213), doi: 10.1126/science.1258096; Charpentier E (2015) CRISPR-Cas9: how research on a bacterial RNA-guided mechanism opened new perspectives in biotechnology and biomedicine *EMBO Molecular Medicine* **7**(4): 363-5.

⁴³⁰ Bacteria comprise the kingdom that includes eubacteria and cyanobacteria. See also Cavalier-Smith T (1998) A revised six-kingdom system of life *Biological Reviews* **73**(3): 203-66.

⁴³¹ Whitman WB, Coleman DC and Wiebe WJ (1998) Prokaryotes: the unseen majority *Proceedings of the National Academy of Sciences* **95**(12): 6578-83.

⁴³² Microorganisms include bacteria, archaea, protozoa, algae, fungi, and viruses.

⁴³³ Cho I and Blaser MJ (2012) The human microbiome: at the interface of health and disease *Nature Reviews Genetics* **13**(4): 260-70.

⁴³⁴ Pennisi E (2014) Modern symbionts inside cells mimic organelle evolution *Science* **346**(6209): 532-3.

⁴³⁵ For example, bacteria have been used to produce plastics, see: Urtuvia V, Villegas P, González M, and Seeger M (2014) Bacterial production of the biodegradable plastics polyhydroxyalkanoates *International Journal of Biological Macromolecules* **70**: 208-13.

conservation and reducing costs when combined with other enabling technologies such as DNA synthesis, microarray analysis, next-generation DNA sequencing, programmable DNA-binding proteins, and 'cell factories'. This is achieved by re-engineering metabolic pathways: the series of chemical reactions, controlled by enzymes, by which cells convert relatively low-cost or toxic inputs into valuable metabolic outputs, such as fuels, high-value chemicals, materials and pharmaceuticals. The particular value of genome editing lies in its potential to facilitate multiple changes necessary to modify a metabolic pathway so that it can work efficiently in this way.⁴³⁶ Applications, however, are not limited to the aims of industrial biotechnology and are of interest to a range of other users operating outside the research fields and institutions that have been considered so far in this report.

Genome editing and synthetic biology

- 7.3 The design and construction of novel artificial pathways, organisms or devices utilising biological materials, or the adaptation of biological systems for a specified purpose describes the field of synthetic biology. This field has developed a distinct identity through the pursuit of defined aims and the adoption of characteristic practices. The aims of synthetic biology comprise the rational design of biological systems according to engineering principles, drawing on disciplines of molecular biology, computer science, chemistry and engineering.⁴³⁷ For its practitioners, these features make synthetic biology conceptually distinct from earlier forms of genetic engineering, such as the development of transgenic plants.
- 7.4 From the point of view of synthetic biologists, genome editing introduces a valuable new set of tools that can be used to modify or design genetic sequences at the level of individual base pairs and, potentially, at multiple sites in a given gene or genome.⁴³⁸ It allows them to test a number of designs or to use the single design-build-test cycle preferred by many synthetic biologists.⁴³⁹ The techniques of genome editing have been enthusiastically embraced by synthetic biologists as Cas9 allows the prolific creation of DNA-binding proteins, and many synthetic biologists are involved in engineering variants of Cas9.⁴⁴⁰ The orthogonal nature (independence) and programmability of the sgRNA/CRISPR-Cas9 pair leads to the possibility of building larger genetic circuits using greater numbers of synthetic regulatory proteins linked to Cas9.⁴⁴¹
- 7.5 Synthetic biologists are self-consciously elaborating a novel field. They see the field as transforming biology as a practical discipline, not only in relation to the adoption of technical innovations, but also epistemically and institutionally (breaking down disciplinary barriers and re-imagining biology as an engineering discipline), and socially and politically (e.g. the desire to build a community and to inculcate certain norms, including those of open source publication and responsible innovation practices).⁴⁴² While, undoubtedly, genome editing has given a fillip to synthetic biology it does not, however, seem to have the same rhetorical significance here as in

⁴³⁶ Response to *Call for Evidence* by the Royal Society.

⁴³⁷ Cameron DE, Bashor CJ and Collins JJ (2014) A brief history of synthetic biology *Nature Reviews Microbiology* **12**(5): 381-90.

⁴³⁸ See, for example, Nielsen AAK and Voigt CA (2014) Multi-input CRISPR/Cas genetic circuits that interface host regulatory networks *Molecular Systems Biology* **10**(11): 763.

⁴³⁹ Response to *Call for Evidence* by the Royal Society.

⁴⁴⁰ Puchta H (2016) Genome engineering using CRISPR/Cas: getting more versatile and more precise at the same time *Genome Biology* **17**:51; "Genome editing is a tool which is an accelerator and catalyst of synthetic biology approaches wherever microorganisms are involved. Genome engineering IS a part of synthetic biology. It is at the very definition of synthetic biology, and discussions about genome editing are directly relevant to synthetic biology" (response to *Call for Evidence*, anonymous).

⁴⁴¹ CRISPR meets synthetic biology: a conversation with MIT's Christopher Voigt, available at: <http://blog.addgene.org/crispr-meets-synthetic-biology-a-conversation-with-mits-christopher-voigt/>.

⁴⁴² In general see: Schyfter P, Frow E and Calvert J (2013) Synthetic biology: making biology into an engineering discipline *Engineering Studies* **5**(1): 1-5; for epistemic distinctness and relation to systems biology, see Nordmann A (2015) Synthetic biology at the limits of science, in *Synthetic biology: character and impact*, Giese B, Pade C, Wigger H and von Gleichen A (Editors), (Cham: Springer), pp 31-58; for an assessment of how far the ideals of synthetic biologists are achieved in practice, see Mercer DW (2015) 'iDentity' and governance in synthetic biology: norms and counter norms in the 'international genetically engineered machine' (iGEM) competition *Macquarie Law Journal* **15**: 83-103.

other areas of biology.⁴⁴³ This might be partly attributable to the fact that the natural reservoir of metaphor for synthetic biology is technical (engineering, construction) rather than textual (editing).⁴⁴⁴

- 7.6 Synthetic biology does, however, offer an insight into possible ways of approaching genome editing as an innovation within research and industry that is essentially different to the translational approaches of biomedicine or, again, public health innovations. Owing, in part, to the different cultures that are integral to synthetic biology (e.g. that of computer science) and in part to lessons about innovation learned from the observation of other fields (e.g. nanotechnology), it has been common for synthetic biologists to adopt responsible innovation practices from the outset.⁴⁴⁵ These tend to see ethical reflection and social engagement as longitudinally integral to their practice ('ethical by design'), as both guiding and governing research, rather than as challenges or decisions to be addressed at particular stages.⁴⁴⁶

Industrial applications

- 7.7 The enthusiasm for genome editing in biotechnology can be understood in the light of its potential value in developing the bioeconomy – those parts of the economy that use renewable biological resources to produce food, materials and energy – especially in replacing depleted or polluting resources such as fossil fuels.⁴⁴⁷ The main industrial applications of genome editing are in the production of simple chemicals or proteins.⁴⁴⁸ Microorganisms have greater genomic plasticity than larger organisms and are easier to engineer. Specific alterations to the genomes of bacteria such as *Escherichia coli* result in changes to metabolic pathways such that they can produce chemicals and proteins that may not be efficiently obtained otherwise through processes such as fermentation. Chemicals include hydrocarbons such as butanol and propane that can replace fossil fuels and petrochemicals.⁴⁴⁹ They also include food additives and flavourings.⁴⁵⁰ Proteins include bioactive antibody segments; for example, *Actinomycetales* is a bacterial order that includes the soil bacteria, *Streptomyces* spp, whose members have the capacity to produce a variety of medically and industrially relevant secondary metabolites: antibiotics, herbicides, chemotherapeutics, and immunosuppressants, such as vancomycin, bialaphos, doxorubicin and rapamycin.⁴⁵¹
- 7.8 One kind of application – again an objective of earlier genetic engineering – is to use modified plants, such as the tobacco plant, or domestic animals (cows, sheep, goats) as biological factories to produce vaccines or other pharmaceutical compounds ('pharming').⁴⁵² These methods of vaccine production may have significant advantages in terms of speed and low cost over production methods that involve growing vaccines in hen's eggs. These advantages could be

⁴⁴³ "Accurate circuit design and metabolic pathway engineering are synthetic biology aims: by providing 'designer nucleases' for engineering (alongside current highly advanced DNA synthesis capabilities), GE has enabled precision engineering of cells with novel pathways and properties. Potential end-points would be those envisaged for synthetic biology", response to *Call for Evidence* by BBSRC and MRC.

⁴⁴⁴ We are grateful to Jane Calvert of the University of Edinburgh (and a member of our earlier Emerging Biotechnologies Working Party) for information about synthetic biology and the observation about the different lexicons.

⁴⁴⁵ On responsible innovation see Stilgoe J, Owen R, and Macnaghten P (2013) Developing a framework for responsible innovation *Research Policy* 42(9): 1568-80. These can be seen reflected to a certain extent in the UK's *Synthetic biology roadmap* (2012), available at: <https://connect.innovateuk.org/documents/2826135/3815409/Synthetic+Biology+Roadmap+-+Report.pdf/fa8a1e8e-cbf4-4464-87ce-b3b033f04eaa>.

⁴⁴⁶ See, for example, <http://www.synbio.ed.ac.uk/responsible-research-and-innovation>.

⁴⁴⁷ For 'bioeconomy' see <https://ec.europa.eu/research/bioeconomy/index.cfm>. See also response to *Call for Evidence* by Vlaams Instituut voor Biotechnologie: "It should not be underestimated how many applications of genome editing in micro-organisms can be foreseen. And these will have a wide variety of applications in (veterinary) medicine, food and feed and industrial applications (the bio-based economy)."

⁴⁴⁸ See, for example, <https://amyris.com/>.

⁴⁴⁹ Kallio P, Pásztor A, Thiel K, Akhtar MK and Jones PR (2014) An engineered pathway for the biosynthesis of renewable propane *Nature Communications* 5: 4731.

⁴⁵⁰ See, for example, <http://oxfordbiotrans.com/products/>.

⁴⁵¹ Tong Y, Charusanti P, Zhang L, Weber T and Lee SY (2015) CRISPR-Cas9 based engineering of actinomycetal genomes *ACS Synthetic Biology* 4(9): 1020-9.

⁴⁵² Shinmyo A and Kato K (2010) Molecular farming: production of drugs and vaccines in higher plants *Journal of Antibiotics* 63(8): 431-3.

particularly significant in emergency situations where there is a strong incentive for swift vaccine development and translation into rapid, large-scale production.⁴⁵³

- 7.9 A benefit of using engineered microorganisms in the production process is the potential to use inexpensive feedstocks, in some cases waste products from other processes or settings, or even just to manage and degrade waste.⁴⁵⁴ These are becoming particularly important applications as environmental protection, mitigation and remediation become more significant policy objectives.⁴⁵⁵

Non-institutional applications

- 7.10 One outgrowth of synthetic biology is the annual international Genetically Engineered Machine (iGEM) competition, which is contested by groups of undergraduate, high school and graduate students.⁴⁵⁶ Each group is supplied with a standard distribution kit and encouraged to design and build genetically engineered systems using standard biological parts (BioBricks).⁴⁵⁷ The competition has a serious purpose: many successful entries advance research in the field and some go on to form start-up companies as a result.⁴⁵⁸ Since 2014 all iGEM BioBrick distribution kits that are sent to registered competitors have contained CRISPR-Cas9 components.⁴⁵⁹
- 7.11 The comparatively low cost and ease of use of the CRISPR-Cas9 system has made it feasible for a greater range of users, beyond those who would ordinarily make use of the techniques of molecular biology. These include those whose purpose is not institutionally-sponsored academic or commercial research: DIY or 'garage' biologists, 'biohackers', and enthusiastic amateurs who are either interested in learning about or experiencing microbiological techniques, carrying out informal research, or making biological products. This prospect has been greeted variously with enthusiasm, cynicism and concern.⁴⁶⁰ A number of sites providing laboratory and ancillary services for amateur microbiologists have sprung up to support the widening interest in microbiology.⁴⁶¹ It is, however, also possible for individuals to pursue this interest in private homes using kits and reagents that are available to order online.⁴⁶² Companies have been established to serve this interest: in 2016 a DIY Bacterial CRISPR kit to render *E. coli* resistant to streptomycin, an antibiotic that is in clinical use, can be obtained for UD\$140 dollars.⁴⁶³

⁴⁵³ See: Nuffield Council on Bioethics (2012) *Emerging Biotechnologies: technology, choice and the public good*, available at: <http://nuffieldbioethics.org/project/emerging-biotechnologies/>.

⁴⁵⁴ "Hypothetically (for example) one could engineer microorganisms to take the CO₂ out of the atmosphere to make carbon-based biofuels which will then release the same amount of CO₂ (but not more) when consumed." (anonymous response to *Call for Evidence*).

⁴⁵⁵ Response to *Call for Evidence* by the Royal Society of Biology.

⁴⁵⁶ http://igem.org/Main_Page.

⁴⁵⁷ http://parts.igem.org/Help:An_Introduction_to_BioBricks.

⁴⁵⁸ http://igem.org/IGEM_Startups.

⁴⁵⁹ See: <http://parts.igem.org/CRISPR>.

⁴⁶⁰ "There is an emerging movement in which people are setting up shops in their garages. Community labs are being set up that allow anyone to come in and be trained. Previously, you had to be an expert in making zinc-finger vectors to edit DNA, but now — because CRISPR-Cas systems are so easy to use — anyone with molecular biology training can do it. On the one hand it is an exciting time for the field because this movement is going to bring in a lot of new ideas and talent. But on the other, it is also going to create new regulatory questions. The democratization of biological engineering is inevitable. Now we have to size up the risks and benefits so we can harness what is going to come of it." Interview with Tim Lu from MIT, Tauxe W (2015) Q&A: Tim Lu. Cocktail maker *Nature* 528(7580): S14. On bio-optimism and bio-pessimism, see Nuffield Council on Bioethics (2012) *Emerging Biotechnologies: technology, choice and the public good*, available at: <http://nuffieldbioethics.org/project/emerging-biotechnologies/>, chapter 1.

⁴⁶¹ The first and perhaps best known of these is Silicon Valley's BioCurious (see: <http://biocurious.org/>). London has Biohackspace (see: <https://biohackspace.org/>). See also Ledford H (2015) Biohackers gear up for genome editing *Nature* 524(7566): 398-9.

⁴⁶² Research interview with professors Drew and Hewinson from APHA.

⁴⁶³ Users of the kit would, however, require additional standard laboratory hardware, which would raise the price of setting up the experiments significantly, if not prohibitively, for the private market. See: <http://www.the-odin.com/diy-bacterial-crispr-kit/> (price as advertised in August 2016).

- 7.12 CRISPR has also been identified as both a possible theme and a medium of expression and cultural intervention for artists and other cultural actors. The late twentieth century saw the rise of bio-art and bio-activism, with practitioners using the techniques and materials of the life sciences to create art and political commentary. Pioneers included Eduardo Kac, Joe Davis, and Marta de Menezes.⁴⁶⁴ Older bioart laboratories such as the University of Western Australia's Symbiotic A have been joined in the twenty-first century by public-orientated laboratory spaces such as California's BioCurious, or the C-LAB art collective. While some bioart has itself been critiqued (for example, the controversy surrounding Kac's green fluorescent rabbit – 'GFP Bunny' – and the suggestion that he was exploiting animals for non-essential purposes), both bioart and the so-called DIYBio citizen science movement have interacted with several research communities and some sectors of the art community as a source of critique of and creative expression within biotechnology.⁴⁶⁵ Common themes include the democratisation of science, drawing attention to dual use, biosecurity, and biological warfare, critiquing the commodification and manipulation of life under neoliberal capitalism, and highlighting eugenic and environmental concerns, as well as more aesthetic and design-centred uses of the techniques of biotech. Bioartists and activists are already interested in the new generation of easy-to-access genome editing tools for creative and political expression.
- 7.13 While it is in the interests of the public to encourage creative and critical engagement with science and technology, given the latter is a major component of contemporary knowledge economies, the perceived potential for inadvertent harm or misuse has heightened concern about whether some techniques should not be freely available outside regulated institutional and/or biomedical contexts. Currently, European DIYBio is considered to be better or more consistently regulated than its US counterpart but there is wide recognition that new genome editing techniques may well be game-changing in their ability to enable of non-institutional actors.⁴⁶⁶

Biosafety

- 7.14 Genetically altered organisms present a theoretical risk of harm to those handling them and, if they escape or are released from laboratories and controlled environments, to other people and to natural ecosystems. Where these organisms are classified as 'genetically modified' there are multiple levels of 'biosafety' regulation relating to handling and releasing them.⁴⁶⁷ Health and safety regulations cover the safety of those working with genetically modified microorganisms (GMMs) and 'larger genetically modified organisms' (GMOs), including any GMOs that pose a significant risk. In the UK, for example, the Genetically Modified Organisms (Contained Use) Regulations 2014 provide for human health and safety, and environmental protection, from GMMs in contained use, as well as human health and safety from GMOs including animals, plants and insects.⁴⁶⁸ Compliance with these Regulations is overseen by the Health and Safety Executive and its inspectorate.⁴⁶⁹ There is cause for greater concern, however, in countries with less well developed infrastructures, where there may nevertheless be significant research funding, where the kits are easily available and many PhD students use them. We heard in evidence claims that the biosafety and biosecurity facilities in some countries can be generally quite poor: the tools

⁴⁶⁴ Yetisen AK, Davis J, Coskun AF, Church GM and Yun SH (2015) *Bioart Trends in Biotechnology* **33**(12): 724-34.

⁴⁶⁵ Myers W (2015) *Bio art: altered realities* (London: Thames and Hudson).

⁴⁶⁶ See Seyfried G, Pei L and Schmidt M (2014) European do-it-yourself (DIY) biology: beyond the hope, hype and horror *BioEssays* **36**(6): 548-51.

⁴⁶⁷ The term 'genetically altered organisms' is used in the preceding sentence to avoid the legal term 'genetically modified organism'; organisms that have been subject to genome editing may fall within or outside the scope of the legal definition of 'genetically modified organism'. For a discussion of the significance of this distinction, see section 5.

⁴⁶⁸ The Regulations transpose and implement European Council Directive 2009/41/EC on the contained use of genetically modified micro-organisms and (unlike the Directive), also cover larger GMOs (animals, plants and insects). See: <http://www.hse.gov.uk/pubns/books/I29.htm>.

⁴⁶⁹ Other elements of the patchwork of health and safety legislation are also relevant to the use of GMOs, including the general requirements of the Health and Safety at Work Act 1974 and associated regulations, and the Control of Substances Hazardous to Health Regulations 2002. The Scientific Advisory Committee on Genetic Modification (SAGCM), an advisory body of the Health and Safety Executive, issues guidance on good practice (prepared in consultation with the Health and Safety Executive) and health and safety inspectors may refer to this in seeking to secure compliance with the law.

might be used inappropriately on an open bench, scientists might become infected, and pathogens may be released.⁴⁷⁰

- 7.15 Transport of genetically modified or potentially hazardous organisms is also covered by legislation that places controls on certain movements and labelling.⁴⁷¹ The Cartagena Protocol is specifically orientated towards technology transfer, providing a mechanism for lower income countries to assert a range of considerations such as public health, economic and environmental benefits and costs when controlling imports of living modified organisms produced by biotechnology.
- 7.16 The release of GMMs and GMOs are covered by national laws and regulations, although principles of environmental protection are given consistency by responsibilities under the Convention on Biological Diversity, and most countries adopt similar procedures including for scientific risk assessments. Regional agreements are particularly important because the spread of genetically altered populations does not respect national borders *per se*.⁴⁷²

Martial applications

- 7.17 As with other biotechnologies there is a potential for military interest in genome editing, although the nature and level of the interest, and of any actual resourcing, is notoriously hard to research due to its secretive nature.⁴⁷³ Areas of potential interest include research aimed at improving battlefield medicine and the acceleration of basic research into physiological and psychological responses to trauma, healing mechanisms and the development of related products and treatments. More speculatively, there is also potential interest in employing genome editing for the enhancement of personnel, in relation to genetic susceptibilities to conditions that they might experience in warfare, improving concentration, and other physiological characteristics such as physical fitness. The most evident security interest, however, is in identifying and countering external threats.
- 7.18 In the UK, the basic biological research that might generate applications of interest to the military and security agencies is funded by the Medical Research Council (MRC) and Department of Health. The Ministry of Defence (MoD) research budget (officially in the range of £400M in 2015/16) is spent almost entirely on applied research. This supports the MoD Defence Science and Technology Laboratory (DSTL), as well as public-private collaborations and R&D in the private sector.⁴⁷⁴ The DSTL runs a human sciences programme, with projects focussed on defence personnel, and a chemical, biological and radiological programme, which, among other things, investigates medical counter-measures to chemical and biological agents ranging from

⁴⁷⁰ Research interview with Professors Drew and Hewinson (APHA). It should be borne in mind that research organisms, as we stated in section 6, are often ideal for research (inbred etc.) but not robust in wild environments as a consequence – the issue here is animals that are edited for release into the wild.

⁴⁷¹ In the UK it is also covered by a variety of legislation applying to the carriage of dangerous goods (the Carriage of Dangerous Goods and Use of Transportable Pressure Equipment Regulations 2009 and the *Accord européen relatif au transport international des marchandises dangereuses par route*, known as ADR) as well as Regulation (EC) 1946/2003 on transboundary movements of GMOs.

⁴⁷² In the EU these include Directive 2001/18/EC on the deliberate release of GMOs into the environment which covers microorganisms when they are not covered by Directive 2009/41/EC on contained use of genetically modified micro-organisms. In the UK, measures are implemented through a sheaf of regulations under the Environmental Protection Act 1990 including the Genetically Modified Organisms (Risk assessment) (Records and Exemptions) Regulations 1996 and The Genetically Modified Organisms (Deliberate Release and Risk Assessment-Amendment) Regulations 1997. Deliberate releases of genetically modified organisms come under the responsibility of The Department for Environment Food and Rural Affairs (DEFRA) England, with Scottish and Welsh Governments being responsible for deliberate releases of GMOs in their respective jurisdictions.

⁴⁷³ We invited senior representatives from the UK Ministry of Defence to participate in a research interview in support of this project but, after informal discussions, this was not taken forward. The difficulty of researching military funding on biotechnologies, and the difficulties that creates for public decision making, is noted in the Council's report on *Emerging Biotechnologies*; see also independent research commissioned to support that project.

⁴⁷⁴ See: <https://www.gov.uk/government/organisations/defence-science-and-technology-laboratory>.

vaccines to protect personnel against infection, to post-exposure treatments.⁴⁷⁵ While genome editing may have many hypothetical uses in military contexts, the official literature is of a very vague and general nature, and what these programmes actually involve cannot accurately be inferred with confidence. Nevertheless the National Security Strategy and Strategic Defence and Security Review 2015 acknowledges the ‘huge potential’ of advances in medical technology, genetic engineering and biotechnology (among other fields, and to which genome editing is arguably now intrinsic) for national security and prosperity.⁴⁷⁶ It also accepts as a fact that controls on access to knowledge and materials will become harder to maintain leading to these technologies becoming available to more state and non-state actors, including terrorists, and organised crime groups. This is explained as a consequence of a reduction of Western states’ ‘technological advantage’ over other actors.⁴⁷⁷ Consequently, there is sensitivity to the emergence of new security threats and an acknowledgement of the need for effective horizon scanning. (The National Security Strategy and Strategic Defence and Security Review 2015 also mentions a new ‘cross-government Emerging Technology and Innovation Analysis Cell’ which will support ‘scouting for new threats’, although this is not more specific than identifying biotechnology as a risk area.⁴⁷⁸)

- 7.19 In the US, the Defense Advanced Research Projects Agency (DARPA) is a major funder of science research (its overall budget for the 2016 fiscal year is officially US\$2.97 billion) and has a dedicated Biological Technologies Office, which exists to exploit the intersection between biology and the physical sciences.⁴⁷⁹ A number of the projects it funds are in the field of synthetic biology and these may be expected to be optimised through the use of genome editing. These projects are typically ambitious and expensive. They include the ‘living foundries’ project, the aim of which is “to create a revolutionary, biologically-based manufacturing platform to provide new materials, capabilities, and manufacturing paradigms for the DoD [Department of Defense] and the Nation”, Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) which aims “to develop and exploit synthetic biology for the *in vivo* creation of nucleic acid circuits that continuously and autonomously sense and respond to changes in physiologic state and for novel methods to target delivery, enhance immunogenicity, or control activity of vaccines, potentially eliminating the time to manufacture a vaccine *ex vivo*”, and Biological Robustness in Complex Settings (BRICS), a translational project based on the ‘living foundries’ to “leverage newly developed technologies for engineering biology towards enabling radical new approaches to solving National Security challenges”. In the US, especially since 11 September 2001, national security applications appear to be a trump card among impact statements for research funding.

Biosecurity and dual use

- 7.20 Much of the military research and military horizon scanning, to which genome editing is potentially relevant and for which public information is available, is concerned with imagining and preparing for the offensive actions that a notional adversary might initiate. Such actions might involve, for example, aggressors obtaining pathogens for deployment against an enemy or civilian population. Biosecurity measures, including controls on access to and use of certain reagents, and monitoring and auditing research, are intended to address such possibilities.⁴⁸⁰ Our evidence collection

⁴⁷⁵ For the human sciences programme, see <https://www.gov.uk/government/publications/human-and-medical-sciences-project-portfolio>; for the Chemical, Biological and Radiological programme, see: <https://www.gov.uk/government/publications/chemical-biological-and-radiological-programme>.

⁴⁷⁶ See:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/478933/52309_Cm_9161_NSS_SD_Review_web_only.pdf.

⁴⁷⁷ *National security strategy and strategic defence and security review* (2015), op.cit. UK Universities are now legally obliged to have in place a ‘PREVENT’ strategy to identify individuals at risk of being radicalised or of inciting radicalisation.

⁴⁷⁸ Ibid.

⁴⁷⁹ For DARPA programme budget see: [http://www.darpa.mil/attachments/\(2G1\)%20Global%20Nav%20-%20About%20Us%20-%20Budget%20-%20Budget%20Entries%20-%20FY2016%20\(Approved\).pdf](http://www.darpa.mil/attachments/(2G1)%20Global%20Nav%20-%20About%20Us%20-%20Budget%20-%20Budget%20Entries%20-%20FY2016%20(Approved).pdf). This includes \$389M on basic research, \$1.2 Bn on applied research and \$1.3 Bn on ‘advanced technology development’.

⁴⁸⁰ Professor Drew said that a major risk was that as an international reference laboratory, APHA may supply reagents for one purpose that are subsequently used for a different purpose. He said that APHA only ever supply reagents to national laboratories and that they are imported only with a licence of the Government of that country, and the APHA ensure that the laboratory is accredited to the biocontainment level appropriate to the pathogen.

revealed concerns that these measures may need to be enhanced since, while the supply of pathogens is carefully regulated, the supply of materials that are needed to manipulate them is not and it is hard for authorities to monitor these activities.⁴⁸¹ In the US, DARPA has launched a project called ‘Improv’ which involves a call to technologists for designs for possible military technologies built exclusively from repurposed software, computer code, and materials that are available to the general public. The aim is to demonstrate the ease with which available resources can be repurposed to present a security risk and to identify likely pathways.⁴⁸² As genome editing systems become available on the open market, their repurposing may become an increasing theoretical source of concern.⁴⁸³

- 7.21 As well as obtaining materiel that can be deployed to cause a security threat, potential aggressors might make use of knowledge from research for offensive purposes. Research that has both civilian and military (or terrorist) uses is known as ‘dual use’ research. The possibility of dual use presents a dilemma: should potentially beneficial research be encouraged in the knowledge that this entails a risk of such knowledge being misused, or should the benefits be foresworn in an attempt to avoid running such a risk? The usual response is not to run towards one horn or the other of this dilemma, although there is often a tension between the security community, with its culture of containment, and the scientific community, which depends on sharing research findings as its lifeblood. The response is usually premised on the expectation that progress in knowledge production may be diverted but cannot ultimately be dammed, and it is therefore preferable for responsible scientists to be at the forefront of research. This, however, may imply the reluctant acceptance of an ‘arms race’ between measures and countermeasures, that entails a necessary tolerance for certain intrusions and limitations on research.⁴⁸⁴
- 7.22 Since it is possible to imagine malicious use for the results of almost all (biological) research, a special subclass of research that, “based on current understanding, can be reasonably anticipated to provide knowledge, products or technologies that could be directly misappropriated by others to pose a threat to public health and safety” (known as ‘dual use research of concern’ – DURC) has been proposed.⁴⁸⁵ The seminal report addressing the dual use dilemma is the US National Academies of Sciences 2004 report, *Biotechnology research in an age of terrorism* (known as the ‘Fink Report’ after its chair, MIT biologist, Gerald Fink). Developing the classification in the Fink report, the US National Science Advisory Board for Biosecurity identified seven categories of knowledge, products or technologies arising from life sciences research that

⁴⁸¹ Research Interview with professors Drew and Hewinson (APHA). It was observed that someone in the UK might be able to obtain from abroad materials to conduct gain of function experiments and that this would be difficult to detect or monitor.

⁴⁸² See: <http://www.darpa.mil/news-events/2016-03-11>.

⁴⁸³ The question of vetting customers for genome editing kits was raised at a roundtable on biosecurity and genome editing held in July 2015 where industry representatives were reassuring that they would only provide kits to bona fide researchers (which may include biohackers supported by a reputable institution). (Biosecu.re, who hosted the meeting, note that a briefing on the interaction between genome editing technologies and the Biological Weapons Convention will be prepared for the treaty’s forthcoming 8th Review Conference in 2016 – see: [http://biosecu.re/biosecure/writing/Entries/2016/5/7_Gene_editing%2C_bioweapons_%26_\(inter\)national_security.html](http://biosecu.re/biosecure/writing/Entries/2016/5/7_Gene_editing%2C_bioweapons_%26_(inter)national_security.html)).

However, one of our research interviews suggested that this was not always the case and that bona fides customer may not always need to be demonstrated and the use to be made of the kits is not always clear to the supplier. (Research interview with APHA).

⁴⁸⁴ Research carried out under the aegis of the UK’s Animal and Plant Health Agency (APHA), for example, manages the possibility of dual use by weighing benefits and risks at the outset, during the life of the project and at publication, and the agency has the option of retaining that information and ensuring that it is not made public. (Research interview with Professors Drew and Hewinson of APHA).

⁴⁸⁵ “Uses of biological technologies and organisms in warfare have waned since the Second World War, likely because biology is stochastic and difficult to control. Nevertheless, all of the microorganisms, animal, and human applications of gene modification technologies are likely to be relevant in military and security contexts,” response to *Call for Evidence* by Angel Petropanagos and Carlos Mariscal. On DURC, see: National Science Advisory Board for Biosecurity (2007) *Proposed framework for the oversight of dual-use life sciences research: strategies for minimizing the potential misuse of research information*, available at: <http://osp.od.nih.gov/office-biotechnology-activities/nsabb-reports-and-recommendations/proposed-framework-oversight-dual-use-life-sciences-research>. See also: Nuffield Council on Bioethics background paper, *Dual use in biology and biomedicine*, prepared by Filippa Lentzos (2015), available at: <http://nuffieldbioethics.org/wp-content/uploads/Background-paper-2016-Dual-use.pdf>.

would indicate a potential for dual use of concern.⁴⁸⁶ Such concerns are addressed through a range of policy measures, such as, in the UK, the joint BBSRC, MRC and Wellcome Trust policy on managing risks of research misuse, that is intended to heighten awareness of risks and is designed to dovetail with the research and institutional governance, and measures to improve the education of researchers about biosecurity and dual use potential.⁴⁸⁷

Box 7.1: Gain-of-function research

A particular source of dual use concern is gain-of-function (GoF) research, such as research into increasing the virulence of disease agents. A frequently cited example is the case of Australian researchers Ronald Jackson and Ian Ramshaw who, in 2001, published a jointly-authored paper exploring the potential control of mice, a major pest in Australia, by infecting them with an altered mousepox virus that would cause infertility. The researchers used a genetic engineering technique to insert the gene for interleukin-4 (IL-4) into the mousepox virus. They found, however that the altered virus had the capacity to kill both mice that were naturally resistant to the ordinary mousepox virus and those that had been vaccinated against it. Publication of their findings in the *Journal of Virology* was followed by complaints that they had provided sensitive information that could lead to the manufacture of biological weapons to potential terrorists who might use the knowledge to create vaccine resistant strains of other pox viruses, such as smallpox, that could affect humans.⁴⁸⁸

Similar controversy surrounded the research into H5N1 flu virus by separate groups in the US and the Netherlands in 2011. This research found that a small number of genetic alterations could enable mammal-to-mammal transmission of the virus by aerosol. Publication was delayed – both research groups agreeing to a voluntary postponement – while security experts and biologists debated the virtues of publishing or suppressing the research. Although no clear consensus was reached, highlighting the different concerns motivating the biological research and security communities, modified versions of both papers were eventually published.⁴⁸⁹

- 7.23 Genome editing has been discussed in the context of a 2015 international inter-academy meeting in preparation for the 2016 8th Review Conference of the Biological and Toxin Weapons Convention (BWC).⁴⁹⁰ The inter-academy meeting report mentions genome editing among developments in science and technology posing future risks for the BWC as a potential means of developing novel agents.⁴⁹¹ From this, a number of areas have been elaborated:

- the use of gene editing tools to produce novel pathogens and/or alter entire populations;
- reduction of risk by removing potential agents from naturally occurring crops e.g. removing the ricin gene from the castor oil plant *Ricinus communis*;
- the difficulty of distinguishing between a ‘natural’ and ‘unnatural’ disease outbreak;
- the lack of ‘fingerprints’ from the use of gene editing techniques may hamper forensic investigations;

⁴⁸⁶ These are knowledge, products or technologies that would: (1) enhance the harmful consequences of a biological agent or toxin; (2) disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification; (3) confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitate their ability to evade detection methodologies; (4) increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin; (5) alter the host range or tropism of a biological agent or toxin; (6) enhance the susceptibility of a host population; and (7) generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent. See: United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (2014), available at: <http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf>; National Research Council (2004) *Biotechnology research in an age of terrorism* (2004), available at: <https://www.nap.edu/catalog/10827/biotechnology-research-in-an-age-of-terrorism>.

⁴⁸⁷ See: BBSRC, MRC and Wellcome Trust position statement on dual use research of concern and research misuse (2015), available at: <https://wellcome.ac.uk/funding/managing-grant/managing-risks-research-misuse>.

⁴⁸⁸ Jackson RJ, Ramsay AJ, Christensen CD, et al. (2001) Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox *Journal of Virology* 75(3): 1205-10. For their reflections on the ensuing furore, see: The mousepox experience (2010) *EMBO reports* 11(1): 18-24.

⁴⁸⁹ See also Nuffield Council on Bioethics (2012) *Emerging Biotechnologies: technology, choice and the public good*, available at: <http://nuffieldbioethics.org/project/emerging-biotechnologies/>.

⁴⁹⁰ Inter-academy partnership (2015) *The Biological and Toxin Weapons Convention: implications of advances in science and technology*, available at: <https://royalsociety.org/topics-policy/projects/biological-toxin-weapons-convention/>.

⁴⁹¹ The transformative potential of advances in life sciences were highlighted in 2014 by the Spiez CONVERGENCE, a foresight workshop series on advances in the chemical and biological sciences and their interaction, of relevance to the Chemical Weapons Convention and the BWC: “The life sciences are advancing at an unprecedented pace, and the amount of data and knowledge acquired is such that non-linear leaps in science and technology should be expected which could lead to a genuine sea change. The wide and rapid impact that the removal of a single obstacle can have, became apparent during the workshop when the use of CRISPR/Cas in genomic editing was discussed.” Spiez Laboratory, the Swiss Federal Institute for NBC-Protection, available at: http://www.labor-spiez.ch/en/akt/pdf/Spiez_Convergence_2014_web.pdf, at page 38.

- the possible use of CRISPR gene drives against wild populations and ecosystems, for example plants or livestock, by actors intent on doing harm;
 - use of gene editing techniques to change the characteristics of an infectious disease so that it resists treatment or controls that prevent it from spreading.⁴⁹²
- 7.24 Specifically, the inter-academy meeting report draws attention to the characteristic absence of distinctive evidence of editing having taken place that may make natural and deliberate events, such as disease outbreaks, difficult to distinguish. This is not the case for gene drives, although they present probably the most significant source of concern.⁴⁹³ Indeed, most respondents to our call for evidence noted that the risks presented by genome editing were not new in kind except, perhaps, in the case of CRISPR-Cas9-enabled gene drive systems although, for the time being, these would probably require the resources of a nation state to deploy offensively.⁴⁹⁴ The UK research councils, accordingly, recognise the possibility for misuse of research but express confidence in robust governance procedures for the research that they support and the applicability of existing regulatory frameworks. They advocate a system “based primarily upon self-governance by the scientific community, but drawing on the inputs of other key stakeholders” as the most effective means of managing risks of misuse.⁴⁹⁵
- 7.25 The viewpoint of the US is somewhat different. It is perhaps a measure of the concern about the unmatched pace of development and diffusion of genome editing – unmatched by parallel developments in governance, policy and culture – that, in February 2016, the US Director of National Intelligence identified genome editing as one of six ‘weapons of mass destruction and proliferation’ in his report on current global threats.⁴⁹⁶ Following this DARPA’s Biological Technologies Office is also sponsoring a ‘Proposers Day’ in advance of a planned Broad Agency Announcement for the Safe Genes Program, initiated in September 2016, with the aim of creating

⁴⁹² Response to *Call for Evidence* by the Royal Society.

⁴⁹³ “Modern genome ‘editing’ technologies, such as CRISPR/CAS-9 often do not leave ‘fingerprints’ indicating that that organism has been altered. This conceals attempts to enhance the organism’s effectiveness, hampers forensic investigations and complicates the differentiation between unusual and unnatural disease events. Some methodologies do leave ‘fingerprints’, in particular, the use of a gene drive as the ability to be passed on to the next generation is due to a permanent change to the organism.” Inter-academy partnership (2015) *The Biological and Toxin Weapons Convention: implications of advances in science and technology*, available at: <https://royalsociety.org/topics-policy/projects/biological-toxin-weapons-convention/>, at page 16.

⁴⁹⁴ “The skills and resources required remain considerable implying that it would likely require the backing of a nation state, however these barriers are likely to be rapidly eroded over the next few years with new technologies.”, response to *Call for Evidence* by the Royal Society. The biosafety and biosecurity “considerations are unlikely to be significantly different in degree or in kind from other R&D using microorganisms, however the consequence of factors such as reduced traceability should be explored.” Response to *Call for Evidence* by Biotechnology and Biological Sciences Research Council (BBSRC) and Medical Research Council (MRC). “Not different from already existing considerations regarding GMOs. Genome editing is not a new concept that requires genuinely new regulations, it has just become more affordable, and technically attainable than ever before. Thus the risks of misuse, which have always existed when genomes were modified, have now multiplied. There is a strong movement to argue that there is no need for further regulation. However it is unclear if all stakeholders will be content with this position. A qualified discussion about the (long) history of genome editing and what has changed (its affordability and technical achievability) will help to put things into perspective.” Anonymous response to *Call for Evidence*.

⁴⁹⁵ See response to *Call for Evidence* by Biotechnology and Biological Sciences Research Council (BBSRC) and Medical Research Council (MRC). This approach is supported by the joint BBSRC, MRC and Wellcome Trust policy on managing risks of research misuse; see: <https://wellcome.ac.uk/funding/managing-grant/managing-risks-research-misuse>.

⁴⁹⁶ “Research in genome editing conducted by countries with different regulatory or ethical standards than those of Western countries probably increases the risk of the creation of potentially harmful biological agents or products. Given the broad distribution, low cost, and accelerated pace of development of this dual-use technology, its deliberate or unintentional misuse might lead to far-reaching economic and national security implications. Advances in genome editing in 2015 have compelled groups of high-profile US and European biologists to question unregulated editing of the human germline (cells that are relevant for reproduction), which might create inheritable genetic changes. Nevertheless, researchers will probably continue to encounter challenges to achieve the desired outcome of their genome modifications, in part because of the technical limitations that are inherent in available genome editing systems.” *Worldwide threat assessment of the US intelligence community* (2016), available at: https://www.dni.gov/files/documents/SASC_Unclassified_2016_ATA_SFR_FINAL.pdf, at page 9.

biological capabilities that enable the safe pursuit of advanced genome editing applications and derivative technologies such as gene drives.⁴⁹⁷

- 7.26 In addition to the offensive possibilities suggested above, a number of more speculative concerns have been suggested, among them that genome editing might lead to the development of ‘smart’ biological pathogens that could affect particular sub-populations selectively or which might be closely controlled.⁴⁹⁸ The application of genome editing to enhance the characteristics or performance of combat personnel, what DARPA refers to as ‘warfighters’, has also been suggested. Concerns expressed here are that the exceptional nature of the martial context might excuse or require exceptional measures, which in any other context would be seen as unacceptable.⁴⁹⁹ As with elite sportswomen and sportsmen, military personnel may therefore be in a position of vulnerability as potential research subjects or put under pressure as employees.⁵⁰⁰ A further possibility is that genetic modification might make it possible to hide messages in biological tissue, allowing people, animals, plants or microorganisms, or products derived from them, to transmit encoded messages across international borders without detection, raising novel challenges for intelligence and security.⁵⁰¹

Moral and societal questions identified

- 7.27 A persistent conceptual question is that of how we should think about or frame the practice of genome editing and its products. On one level this might look, at present, like a domestic question of disciplinary taxonomy for universities and research institutes, except that genome editing shows the potential to disrupt disciplinary formations and their associated forms of organisation, administration and governance. The emergence of synthetic biology suggests how this may happen within the life sciences, although the uses of genome editing exceed the field that synthetic biology has marked out. Thinking about genome editing from the point of view of an established disciplinary knowledge culture may be less appropriate, therefore, than thinking about it in relation to the (expanding number of) contexts and conditions in which it is used. This leads to at least two problematic practical consequences.
- 7.28 The first relates to how the products of genome editing are taken up into existing governance and regulatory frameworks. The question of whether the product of genome editing is a GMO for the purposes of regulation is not inconsequential – it may determine, for example, the applicability of the Cartagena Protocol and its associated procedures – but it is only the most obvious manifestation of the more profound question of the moral and social significance of the genome editing procedure itself, of the different kinds of interventions that it may enable, and the possible outcomes that are perceived to associate with them. (A similar issue was noted in relation to food and agriculture in section 5.) On the supply side there are potentially very few controls: in interview, a representative of a company supplying genome editing products and services suggested that no procedure existed for verifying the *bona fides* of those to whom they provided products or services (e.g. modified animals, CRISPR editing kits) and that to do so would not be

⁴⁹⁷ This programme was announced shortly before initial publication of this report and little information was publicly available at that time; see: <http://www.darpa.mil/news-events/2016-09-07>.

⁴⁹⁸ “The ability to design and edit a pathogen also raises the possibility of attempting to identify genomic targets (and design specific countermeasures) or to design-in time-limited effects or other means to neutralise a biological agent (i.e. means which might make the weapon appear more controllable and make its use more imaginable).”, response to *Call for Evidence* by David Albert Jones.

⁴⁹⁹ Agamben G (2005) *State of exception* (translated by Attell K) (Chicago: University of Chicago Press).

⁵⁰⁰ ‘Gene doping’ has been on the list of banned doping practices of the World Anti-Doping Agency (WADA) since 2003, although no evidence of its use has yet emerged. See also Wired (28 July 2016) *Olympic drug cops will scan for genetically modified athletes*, available at: <https://www.wired.com/2016/07/olympic-drug-cops-will-scan-genetically-modified-athletes/>; response to *Call for Evidence* by Angel Petropanagos and Carlos Mariscal.

⁵⁰¹ Response to *Call for Evidence* by Angel Petropanagos and Carlos Mariscal. DNA is an efficient store of information: in 2012 George Church announced that he had encoded his 2012 book *Regenesis: how synthetic biology will reinvent nature and ourselves in DNA* (co-written with Ed Regis) in DNA; the book was approximately 53,000 words (about the length of this report) including images, and Church and his collaborators produced about 70 billion copies of it in the process (considerably more than the print run of this report). See Church GM, Gao Y and Kosuri S (2012) Next-generation digital information storage in DNA *Science* 337(6102): 1628. See also: Extance A (2016) How DNA could store all the world’s data *Nature* 537(7618): 22-4.

usual, given that the products were approved by the appropriate regulator (in this case the FDA).⁵⁰² Genome editing appears to have made distinctions more difficult, both to draw and to enforce, between 'safe' and 'unsafe' in relation either to the technologies or to their users.

- 7.29 The second practical problem relates to the circumscription of a 'community' of users or practitioners as correspondents in a notional system of moral injunctions and responsibilities, and subject to professional or institutional control and sanction. Whereas the cultural response of the elite 'scientific community' is typically enjoined by a sense of common responsibility, this notion of community may be becoming increasingly attenuated. Beyond the class of elite academic research scientists there is a growing class of scientific professionals and technicians, and, beyond these, a demi-monde of scientifically literate but not scientifically socialised ('disciplined') amateurs and dilettantes, with a variety of interests in genome editing, not all of which may be defined by the pursuit of knowledge 'for the relief of man's estate'.⁵⁰³ Significantly, in the present case, the very accessibility of genome editing itself may have the potential to undermine the coherence of the community by extending the opportunities of inquiry and technology to those to whom they were previously inaccessible behind barriers of recondite knowledge, unaffordable resource requirements, or membership of a group with strict and technologically meaningful rites of passage. While it may be the case that self-regulation is sufficient for risks that still require the resources of a nation state to realise, this may not continue always to be the case. It might be appropriate to question not what the scientific community can do to recuperate genome editing for itself but what implications the flourishing of accessible techniques in the life sciences might have for the integrity of the hitherto existing scientific community and its power to self-regulate. While the response to this, of the sort that synthetic biologists have self-consciously explored, may lie in the formation of novel sorts of reflective, socially engaged and self-regulating communities (which overrun distinctions between knowledge formations while simultaneously reviving exuberant experimentalism) it is doubtful that it can rely on *discipline* in the conventional academic sense, which requires a defined community of practitioners.⁵⁰⁴
- 7.30 The overflowing of life science into non-elite discourse and practice, and the speed and promiscuity with which research tools are deployed, characteristic of synthetic biology, has been celebrated by enthusiasts as a 'democratisation' of science. The scale (or scalability) of the technologies probably makes a significant difference here, with biology arguably moving from 'big science' like the Human Genome Project to a handheld scale, at the same time harnessing the accessible design facilities of digital computing in place of wet bench experimentation.⁵⁰⁵ It is also facilitated by social developments such as the broadening of access to higher education and to academic conferences, and the spread of information via the internet (and the 'dark web'), and cultural movements within science, such as 'open' publishing and 'open data'. Another factor is the intervention of Silicon Valley-style market capitalism (with crowdfunding flowing into the spaces not taken by venture capitalists) in the innovation system.⁵⁰⁶ This raises the question of whether such developments might encourage what economists would call 'market failure' (inefficient allocation of resources) and the production of 'negative externalities' (social costs and harms) that, many would argue, require some form of public regulation. If failures of this kind can be identified or foreseen, and regulation is the correct response, this leads to questions about

⁵⁰² Research interview with Ruby Yanru Chen-Tsai, Applied Stem Cell, Inc.

⁵⁰³ See section 3. Even within the academy, as our work on *Research Culture* shows, the cultural gap between tenured professors and the ranks of postdocs is not diminishing. Concerns about the impact of workload, competition and career structures on early career researchers were reported as factors felt most to threaten the quality and integrity of science.

⁵⁰⁴ "High levels of awareness, and appropriate and robust behavioural norms in the science community are vital to ensure that knowledge and wisdom in its humanitarian use develop together. Training and professional standards will be important and particular attention to the sharing of information and resources." Response to *Call for Evidence* by the Royal Society of Biology.

⁵⁰⁵ For scale of DNA analysis see Check Hayden E (2015) Pint-sized DNA sequencer impresses first users *Nature* **521**(7550): 15-6.

⁵⁰⁶ The ODIN, for example, which makes 140 US dollar CRISPR kits, was set up with crowdfunding in December 2015 – the majority of the 290 backers put in a level of funding equivalent to the cost of the kit (see: <https://www.indiegogo.com/projects/diy-crispr-kits-learn-modern-science-by-doing#/>).

what kind of regulatory governance mechanisms can be put in place, and have meaningful traction, given potential for the wide variation and geographical dispersal, at times, into relatively uncontrolled environments.

- 7.31 A related concern is the potential ‘democratic deficit’ with regard to both the social orientation of research and innovation, and the equitable distribution of benefits. This raises, once again, profound but persistent questions about the preference for, or acceptance of, contingent structural features of innovation systems (like relationship of public and private sector actors involved), which are particularly pertinent at a time when such systems are confronting technological change that is both rapid and of significant potential impact.⁵⁰⁷ On one view, the power of research and innovation profoundly to affect the conditions of common existence, and the equitable distribution of costs and benefits, entails a responsibility to society that cannot be divined through market signals, which are too ambiguous, too unequal and too late.⁵⁰⁸ Such objections run up against the view that there must be proper limits to intrusion to protect the freedom of inquiry which is necessary for science to refresh itself and develop, and to avoid repeating the historically poor performance of *dirigiste* policies and regimes, as well as the possibility that, however flawed, market signals may be the most workable solution in the circumstances.⁵⁰⁹ Whatever the optimum form of governance, the major consideration for this report has been the speed of development and diffusion of the techniques of genome editing relative to the social processes by which normative frameworks, such as those of law, regulation and public acceptance evolve. The possibility of attenuation or fracture of this relationship between the scientific and normative knowledge warrants further examination.⁵¹⁰

Conclusion

- 7.32 As in most areas that we have considered, the major impact of genome editing derives from the broad applicability, speed, efficacy and accessibility of the techniques. In industrial applications genome editing promises to further the existing aims of conventional genetic engineering and synthetic biology. It is complicated, however, by the fact that the accessible features of genome editing may themselves exacerbate the transformation of research from a relatively elite activity, removed to academic institutions and industrial corporations, to something that is open, diffused and integrated with technology and markets. This is compounded by the speed of development, which potentially places stress on the relationship between scientific knowledge and technical capacities, and the normative frameworks within which they are applied.
- 7.33 A distinct set of issues concerns research that has potential military or terrorist applications. Although genome editing does not generally raise issues that are different in kind from previous research, the fact that genome editing makes the implementation of this research easier is a matter for serious consideration (for example, in relation to the Biological and Toxin Weapons Convention). New possibilities raised by convergence of genome editing and gene drive technologies may become a matter of increasing concern as the technologies develop. There are also other issues in a military context that require monitoring, such as the vulnerability of military personnel as potential research subjects and the question of legitimate enhancement.

⁵⁰⁷ These issues were also covered in *Emerging Biotechnologies*. The question may be formulated as the dilemma of *dirigisme* or *laissez faire* over which successive governments have vacillated.

⁵⁰⁸ “Scientists need to be responsible to society: It may be beneficial for those who wish to pursue a career in this field [gene-editing], especially those who oversee or direct laboratory research to undertake training or a period of sustained advanced-learning that goes ‘beyond ELSI’ [Economic, Legal and Social Issues] to cover ‘PEELSA-ST’ (political, economic, ethical, legal and social aspects of science and technology) (see Calvert et al. 2015). Scientists themselves must be enabled through reflexive tools and social theory to critically assess the ways in which their work or innovation meets the needs of society, and reflect upon who defines those needs and why and whose needs are or are not considered? This will allow researchers to better engage and deliberate with ethicists, social scientists, stakeholders, various publics and policy makers about the socially desirable orientation of research and innovation,” anonymous response to *Call for Evidence*. See also: Balmer A, Calvert J, Marris C, et al. (2015) Taking roles in interdisciplinary collaborations: reflections on working in post-ELSI spaces in the UK synthetic biology community *Science and Technology Studies* **28** (3): 3-25.

⁵⁰⁹ “It is in turn important that scientists be allowed the contained spaces to pursue basic research unhindered (to the extent possible) by overriding concerns for public acceptance or commercialization. Scientists should also be allowed to carry out fundamental research without fear for their personal safety”, anonymous response to *Call for Evidence*.

⁵¹⁰ See section 2 above.