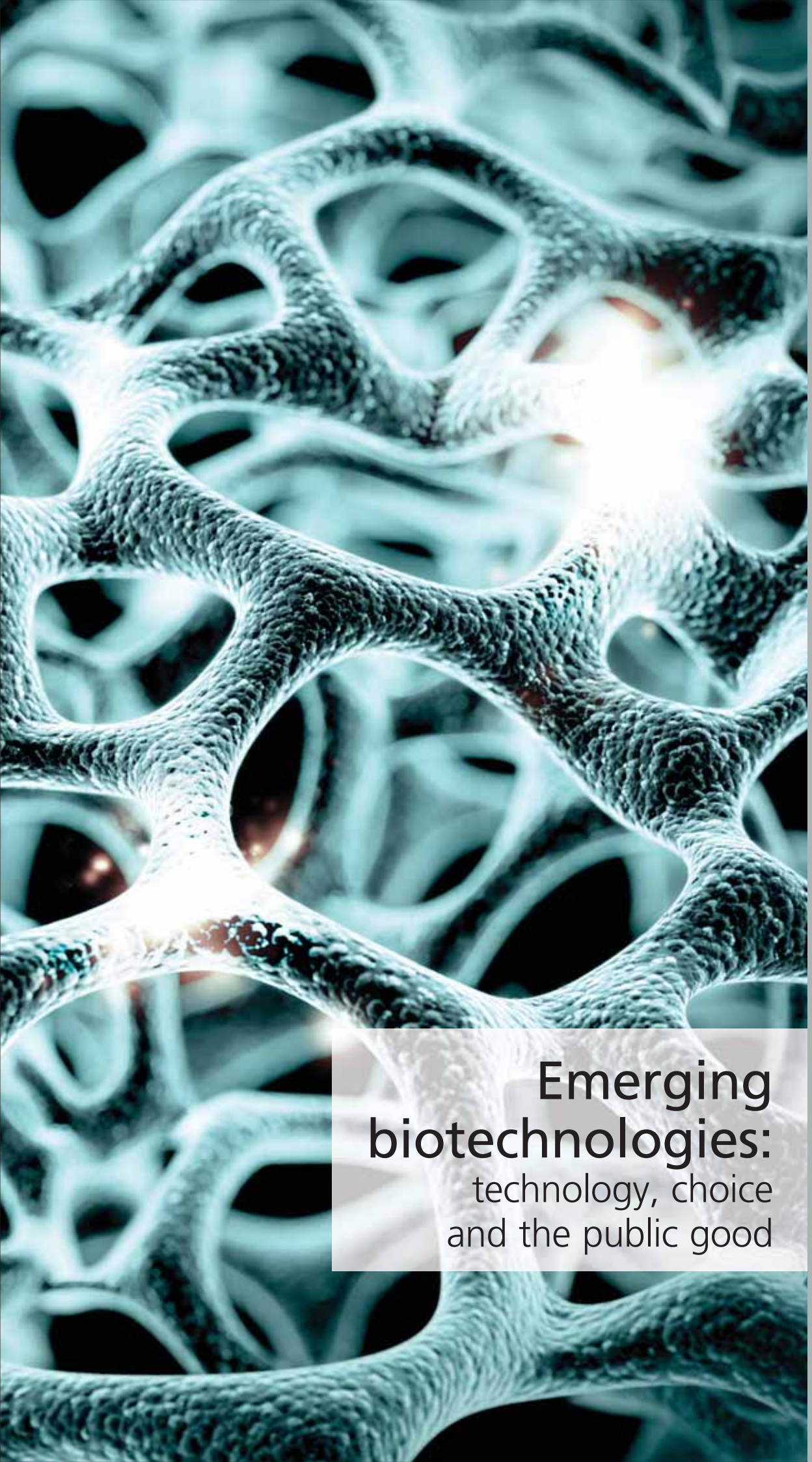

Emerging biotechnologies:
technology, choice and the public good

NUFFIELD COUNCIL ON BIOETHICS

Published by
Nuffield Council on Bioethics
28 Bedford Square
London WC1B 3JS

Telephone: 020 7681 9619
Email: bioethics@nuffieldbioethics.org
Website: http://www.nuffieldbioethics.org

ISBN: 978-1-904384-27-4

December 2012

To order a printed copy, please contact the Nuffield Council on Bioethics or visit the website.

£10 per report (where sold)
Developing countries: Free

Web references throughout this report were accessed December 2012

Printed in the UK by:
ESP Colour Ltd.
Elgin Drive
Swindon
Wiltshire
SN2 8XU
http://www.espcolour.co.uk

Printed using vegetable based inks on FSC® certified paper. The printer holds the environmental standard ISO 14001.

Emerging biotechnologies: technology, choice and the public good

Nuffield Council on Bioethics

Professor Jonathan Montgomery (Chair)

Professor Thomas Baldwin*

Dr Amanda Burls

Professor Robin Gill

Professor Sian Harding

Professor Ray Hill

Dr Rhona Knight**

Professor Graeme Laurie

Dr Tim Lewens

Professor Ottoline Leyser (Deputy Chair)

Professor Anneke Lucassen

Professor Michael Moran***

Professor Alison Murdoch

Professor Bronwyn Parry

Professor Nikolas Rose

Dr Geoff Watts

Professor Jonathan Wolff

* co-opted member of the Council while chairing the Working Party on Novel neurotechnologies: intervening in the brain.

** co-opted member of the Council while chairing the Working Party on Donor conception: ethical aspects of information disclosure.

*** co-opted member of the Council while chairing the Working Party on Emerging biotechnologies: technology, choice and the public good.

Secretariat

Hugh Whittall (Director)

Dr Peter Mills

Katharine Wright

Emily Postan

Catherine Joynson

Sarah Walker-Robson

Tom Finnegan

Kate Harvey

Rosie Beauchamp

Carol Perkins

Ranveig Svenning Berg

Johanna White

The terms of reference of the Council are:

1. to identify and define ethical questions raised by recent advances in biological and medical research in order to respond to, and to anticipate, public concern;

2. to make arrangements for examining and reporting on such questions with a view to promoting public understanding and discussion; this may lead, where needed, to the formulation of new guidelines by the appropriate regulatory or other body;

3. in the light of the outcome of its work, to publish reports; and to make representations, as the Council may judge appropriate.

The Nuffield Council on Bioethics is funded jointly by
the Medical Research Council, the Nuffield Foundation, and the Wellcome Trust

Acknowledgments

The Council wishes to extend its thanks to the members of the Working Party for their time, hard work, expertise and contributions to the report. In addition, the Council would like to thank those who attended the various fact-finding meetings held by the Working Party and all those who responded to the consultation. Particular thanks should be extended to those who agreed to act as external reviewers for an earlier draft of the report, who provided so much insightful guidance and commentary. Further detail on these processes – and people – can be found in the Appendices.

The Working Party commissioned two illuminating reports concerning important elements of the project: an explanation of the significance of the concept of 'emergence' in the UK patent system, and a review of what information could be obtained about the sources of funding for the research and development of biotechnologies. For these two reports we would like to thank, respectively, Dr Siva Thambisetty of the Department of Law, London School of Economics and Political Science and Dr Michael Hopkins of SPRU (Science and Technology Policy Research), University of Sussex.

Finally, we wish to thank Kate Harvey of the Nuffield Council on Bioethics Secretariat for her work in helping to complete the production of the report.

Foreword

1 The use of living organisms, biological components and biological processes to create useful products has applications in almost every field of human activity that is important to our wellbeing and way of life, including medicine, industry and agriculture. The Nuffield Council on Bioethics first began to look at examples of these technologies in 2009, taking as its focus the fields of synthetic biology and nanotechnology. The Council quickly became convinced that these and other examples of emerging biotechnologies raised similar or related ethical issues that could profitably be considered together.

2 When we began to look at the field of emerging biotechnologies, however, their sheer breadth became apparent and their differences perhaps more important than their similarities. The only cross-cutting issue common to all emerging biotechnologies is indeed that they are 'emerging'. Therefore we have focused precisely on this process of emergence, and on the conditions that shape it. We are concerned, above all, with how reflection on decisions concerning biotechnology innovation can produce outcomes better aligned with the public good.

3 Our report is offered in this spirit of reflection. It does not offer a template of particular recommendations, but a set of principles by which our society may better think about, and discuss, the making of biotechnology choices.

4 On a personal note I would like to offer my thanks to the Members of the Working Party for their hard work and creativity over 11 meetings in 18 months. I am sure that members of the Working Party will also want me publicly to thank the members of the Council, especially the subgroup of Members who provided valuable feedback and guidance on successive drafts. A huge debt is owed also to members of the Secretariat who have borne the brunt of the work involved in preparing the report. Special thanks are due to two members of the Secretariat, Peter Mills and Tom Finnegan, for their unfailing patience, hard work beyond the call of duty and creative intellectual engagement with the complex issues discussed in these pages.

Michael Moran, December 2012

Members of the Working Party

Professor Michael Moran (Chair)
Professor Emeritus of Government, University of Manchester

Dr Jane Calvert
Reader in Science, Technology and Innovation Studies, ESRC Innogen Centre, University of Edinburgh

Mr Trevor Cook
Partner, Bird & Bird LLP

Professor David Edgerton
Hans Rausing Professor and founding director of the Centre for the History of Science, Technology and Medicine, Imperial College London

Professor Ray Hill
Head of Licensing and External Research for Europe, Merck, Sharp and Dohme until his retirement in May 2008; Visiting Professor, Imperial College London, Bristol, Surrey and Strathclyde Universities; President Emeritus of the British Pharmacological Society

Professor Søren Holm
Professor of Bioethics, University of Manchester; part-time Professor of Medical Ethics, University of Oslo, Norway

Professor Richard A.L. Jones
Pro-Vice-Chancellor for Research and Innovation, University of Sheffield

Professor Eli Keshavarz-Moore
Professor of Bioprocess Science and Enterprise, University College London

Professor Noel Sharkey
Professor of Artificial Intelligence and Robotics and Professor of Public Engagement, University of Sheffield

Professor Andrew Stirling
Professor of Science and Technology Policy and Research Director, SPRU (Science and Technology Policy Research), University of Sussex

Professor Patrick Sturgis
Professor of Research Methodology, University of Southampton; Director, ESRC National Centre for Research Methods

Professor Andrew Tylecote
Emeritus Professor of the Economics and Management of Technological Change, University of Sheffield

Terms of reference

1. To examine common social, ethical and legal issues raised by emerging biotechnologies, in particular the implications for policy, governance and public engagement.

2. To explore issues of benefits, harms, risk, precaution, uncertainty, public perception and intellectual property related to emerging biotechnologies.

3. To consider the above areas in light of the historical and social context in which biotechnologies have in the past developed and been received and managed.

4. To draft a report and make recommendations on research, policy, governance and public engagement.

Table of Contents

Summary

Introduction

1. This report falls into two parts. The first identifies features and challenges that are common among emerging biotechnologies, and develops an ethical approach for responding to these. It shows that 'emerging biotechnologies' are, in reality, a diverse collection of research programmes, forms of knowledge and techniques, although they encounter similar issues when they confront the practical conditions of research and innovation systems. On one hand, we distinguish *emerging* biotechnologies from established biotechnologies or those in later phases of development by highlighting the particular problems attached to 'emergence'. On the other hand, we distinguish emerging *bio*technologies from other emerging technologies by virtue of the particular issues of public interest they raise.

2. The second part of the report examines how these features of emerging biotechnologies generate difficulties within a number of different contexts – research, policy, regulation and business – and how responses to these, in turn, shape their emergence. It suggests how the ethical approach developed in the first part might be used to improve the integration of these contexts with each other and with otherwise excluded perspectives, in order to improve the ethical quality of biotechnology governance.

The Biotechnology wager (Chapter 1)

> Choices about how different biotechnologies are supported and governed have significant consequences for the pursuit of national priorities and meeting global challenges in healthcare, food, energy, the environment and the economy. But prospective biotechnologies will not necessarily develop along predictable paths. They emerge in a complex set of conditions and constraints, only some of which can be foreseen or controlled.

3. Biotechnologies already play a significant role in many areas fundamental to human wellbeing, including food and energy production, medicine, industry and intellectual capital. Although they have been responsible for substantial benefits, the historical impact of biotechnologies has not been uniformly positive. Nevertheless, as a society we place significant investment in prospective biotechnologies to increase future wellbeing, while at the same time providing remedies for the accumulated negative impacts of previous technologies. The 'biotechnology wager' refers to the way in which we are not only 'betting' on biotechnologies against other responses to the challenges we collectively face, such as climate change, food and energy security, but may even be depending on the success of future innovations simply to offset the costs of previous consumption and maintain current standards of welfare.

4. The 'wager' represents only one of a number of possible attitudes towards emerging biotechnologies. The full spectrum of attitudes ranges from whether biotechnologies will have substantial or only relatively minor impacts, and also whether those impacts will be ultimately beneficial or harmful. Reviewing the successive evaluations of past technologies it can be seen that conclusions about their impacts and utility are subject to change and revision throughout the lifetime of a technology and beyond.

5. We characterise the emergence of biotechnologies as a process of bringing together knowledges, practices, products and applications into productive conjunctions. This is a complex process that is poorly understood and difficult to model, even in retrospect. It is highly dependent on the development and innovation context and not merely on the quality of the underlying science. What can be learned from previous technologies is of limited assistance in predicting the evolution of emerging biotechnologies and can even be misleading, owing to problems of selection bias (the evidence we have is largely of the small number of inventions that developed successfully rather than the greater number that did not) and relevance (prospective technologies

may be significantly different from past technologies especially where the underpinning science is novel and its limitations untested).

6. Nevertheless, expectations of emerging biotechnologies still tend to be informed by implicit models formed on the basis of these selective experiences. We argue that such models tend to focus (inappropriately) on the potential power of the technologies themselves rather than the circumstances of their emergence. This focus may draw attention away from a balanced consideration of alternative approaches and opportunity costs, considerations that are of great importance at a social level. We conclude that taking a broad view of biotechnology as a matter of social choice requires consideration of a range of alternatives that are often absent in current technology governance. This conclusion informs our approach in this report as well as our more general advice that **commitments to particular technological pathways should be evaluated not only in terms of their expected future impacts but also by comparison to possible alternative pathways; this can help to illuminate obscured assumptions, constraints and mechanisms of the innovation system, and help to identify sites and opportunities for more constructive governance, prioritisation and control**.

Biotechnology promises and expectations (Chapter 2)

There is often a mismatch between our expectations of emerging biotechnologies and our experience of biotechnology emergence. Policy and governance are nevertheless strongly informed by expectations and visions of the future. This underlines the importance of focusing on the way in which emerging biotechnologies are represented in the contexts in which key decisions are made.

7. The term 'biotechnologies' covers a broad range of activities that are related through the fact that they involve the creation, manipulation or use of 'biological' components but may not otherwise share any feature in common. 'A biotechnology' may denote different kinds of thing, from broad fields of knowledge to particular products. The range of applications of biotechnology is also broad (including medicine, agriculture and food production, environment and industry) and a single 'biotechnology' may cut across many of these.

8. We briefly survey the recent history of biotechnology research in some key areas. These include:

   - cellular biotechnologies and regenerative medicine, for example: stem cells for transplant and disease modelling;
   - genetic engineering, for example: modification of agricultural crops and transgenic animals for 'pharming' and xenotransplantation;
   - pharmaceutical biotechnology, for example: recombinant proteins (such as biosynthetic insulin) and monoclonal antibodies (such as trastuzumab ('Herceptin'®) used to treat breast cancer), as well as RNA interference to regulate gene expression;
   - personalised medicine, for example: pharmacogenomics and the convergence of medicine with information and communications technology (ICT) applications;
   - synthetic biology, for example: parts-based approaches, metabolic pathway engineering, minimal genome and protocell research, and xenobiology; and
   - biological applications of nanotechnology, for example: biological machines, molecular motors, drug delivery devices and biosensors.

9. We note that emerging biotechnologies are promissory by nature and that ambition and expectations play an important role in securing the material conditions (including funding) that enable advances to be made. Analogies with other technological forms, for example information and communications technology, provide a powerful template for imagining the future development of emerging biotechnologies, not least because of convergence between biology and ICT in interdisciplinary fields such as systems biology. Their familiarity can help to inform non-specialist understanding of new and complex technical fields.

10. However, many technologies fail to fulfil their initial promise (either due to encountering a 'hard constraint' or being 'crowded out' by an alternative technology); they may remain 'submerged' for long or indefinite periods, or find wholly different applications from those originally envisaged. Of course, there are also genuinely transformative technologies that may exceed expectations or

create new markets or fields of application, and others that are not preceded by expectations because they arise unexpectedly in the context of use rather than through prior research or deliberate design.

11. We identify a cause for concern in the possibility that proposed pathways to imagined futures can become aligned with political interests, to the extent that resistance to a particular biotechnology initiative may be derided as 'anti-science'. At the same time, conditions may be created in which excessive promising can become an accepted part of the way researchers secure support for their research.

The threefold challenge of emerging biotechnologies (Chapter 3)

> Emerging biotechnologies are characterised by uncertainty, ambiguity and transformative potential. These characteristics make it difficult to arrive at a universal rational basis for commitment to particular biotechnologies, areas of biotechnology or indeed biotechnology at all, as means of pursuing social objectives. These characteristics should be explicitly recognised when commitments to biotechnology pathways are being considered.

12. We identify three characteristics that distinguish emerging biotechnologies from biotechnologies more generally.

13. The first characteristic is *uncertainty* about the range of possible outcomes from a given biotechnology or the likelihood of each coming about. Uncertainty is distinguished from quantifiable risk, where both the range of outcomes and the likelihood of their occurrence are predictable with a reasonable level of confidence. This distinction has important consequences for how decision making should be approached. Under conditions of uncertainty, emphasis shifts from the attempt to select the optimum pathway for biotechnology to fostering diversity of technological development, flexibility to move commitments among different technologies and precaution in innovation.

14. The second characteristic is *ambiguity* of meaning and value attached to the practices, products and outcomes of emerging biotechnologies. Even if the outcomes of various commitments to biotechnologies could be predicted with reasonable confidence these may still be understood and valued differently from different perspectives or in different contexts. The use of biological materials and systems may also have a different significance to different people. Finally, the generation novel objects not found in nature can disturb schemes of meaning and value, through ambiguity about how they relate to more familiar 'natural' phenomena. The assignment of any single framework of values to biotechnology decisions may therefore be socially contested.

15. The third characteristic is the *transformative potential* of emerging biotechnologies. The capacity of biotechnologies to produce profound changes in their social, commercial or physical environments, may have significant implications for shared ways of life, not only for the 'users' of those technologies but for all members of society. These are not merely technical or economic impacts but also social and ethical ones (for example, where social groups become inured to previously unwelcome practices). The potentially pervasive and irreversible nature of such transformations underscores the importance of opening up reflection about foregone pathways and opportunity costs.

16. These three characteristics create substantial difficulties in making decisions about what resources to commit to particular technological pathways or even to broad areas of research. We argue that typical responses to this tend to involve narrowing decisions around only selected aspects (such as potential for delivering economic growth), thereby failing to take account of broader concerns about the value of common social life and the public good. We draw attention to how the 'framing' of decisions in this way has consequences for the shaping both of technologies and social conditions.

Public ethics and the governance of emerging biotechnologies (Chapter 4)

Public interest in emerging biotechnologies suggests that they should be subject to a 'public ethics' rather than the protection of different individual interests. This can be put into practice as a 'public discourse ethics' through the cultivation of a number of important procedural and institutional virtues. Public discourse ethics offers a practical way of responding collectively to the threefold challenge of emerging biotechnologies through 'public' decision making, orientated by pursuit of the public good.

17. In this chapter we argue for a new 'public ethics' approach to biotechnology governance. The need for such an approach arises from the significant public interest in biotechnologies. There are several sources of this interest, some of which are common to other technologies.

18. One source lies in the potential of biotechnologies to create significant benefits and harms as a result not only of intended uses but also as a result of misuse, unintended consequences and associated uncertainties and ambiguities. These harms often occur at a public scale from which individuals cannot 'opt out' or be excluded.

19. The development – not merely the use – of biotechnologies gives rise to morally relevant considerations. Biotechnologies involve public goods (such as scientific knowledge) that are not typically provided efficiently by market mechanisms but usually require public provision. A second source of public interest therefore lies in the decision to support certain sorts of public goods and in the fair and effective use of public resources to do so.

20. A third source of interest arises from the distinctive significance that is attached to living things, whether this is because of sensitivities to religious and cultural attitudes, the extent of human interdependence with them, limitations of human understanding or control over biology, or the particularly sensitive structural and dynamic features of biological systems (and their potential for catastrophic effects).

21. A fourth source of interest is in the potential for certain technologies in use to affect social relations and to shape the conditions of common life in non-trivial ways, potentially changing the future options available to all in ways that may favour only some.

22. We emphasise that there is a positive moral value in developing biotechnologies to avoid or alleviate harms, and to increase human welfare and well being. However, this value should be applied consistently across possible alternative visions that guide public decision making. We propose three underlying values that will help to orientate the pursuit of wellbeing and avoidance of harm towards the public good rather than towards the private good of sectional interests:

    - Equity
    - Solidarity
    - Sustainability

23. In a plural society there will not be a single vision of the public good that can be applied in all circumstances. We propose that in relation to the governance of emerging biotechnologies the public good should be fostered through a 'public discourse ethics'. This takes place as an encounter between different ways of framing the biotechnology decisions in question. What characterises 'public' discourse in this sense are the qualities of *non-privacy* (not being carried out in isolation from public influence or scrutiny) and *non-partiality* (not being framed by private or sectional interests). We conclude that public discourse ethics should be encouraged through the cultivation of a number of procedural and institutional virtues. These are:

    - Openness and inclusion
    - Accountability
    - Public reasoning
    - Candour
    - Enablement
    - Caution

Public perspectives (Chapter 5)

The governance of emerging biotechnologies in accordance with public ethics involves an engagement between different values, understandings and visions. All approaches to public engagement have advantages and limitations, and while such engagement can be highly beneficial, we recognise that decisions about the conditions under which engagement takes place always involve dilemmas.

24. We discuss the meaning of 'the public' and 'publics' as distinct from those with authority to make decisions about biotechnology policy and governance. 'Public perspectives' in this sense are those held by a range of social actors. We distinguish a number of rationales for engaging public perspectives and discuss how the rationale may determine how any particular initiative comes to be evaluated. We examine how public engagement may contribute to more robust public decision making with regard to emerging biotechnologies.

25. In interdisciplinary questions of the sort with which biotechnology governance is concerned engagement beyond traditional scientific elites can act as a counterbalance to technical interests and cultures (such as a tendency to place undue weight on the pursuit of rapid advance at the expense of confidence in the robustness of knowledge).

26. We note major distinctions between methods of public engagement, drawing attention to the need to tailor the method to the specific context and the fact that all methods have both advantages and limitations. We conclude that there is no single 'best' method of public engagement and that the choice of approach will always involve dilemmas. Issues of selection and design are – and should always be acknowledged to be – conditional on underlying purposes and objectives. If the approaches used are poorly aligned with underlying objectives, the result may be poorer rather than better quality outcomes.

27. We set out a number of dilemmas that arise in public engagement. The first of these concerns the implications for 'upstream' engagement in relation to emerging biotechnologies, where both the underlying science and prospective applications are often obscure. Here the dilemma is created by an unwarranted expectation that the future can be predicted, and that the mechanisms through which it is produced are understood. The value of upstream engagement is in understanding the scope of the different values and interests at stake, and their associated aims and visions.

28. A second dilemma arises from a tension between the tendency of engagement to multiply questions and the needs of decision makers to find answers that justify particular decisions. In order to encourage understanding of plural perspectives while respecting accountability for decision making we recommend that **expert deliberation and public engagement exercises should report their conclusions not in the form of simple prescriptive findings but as properly qualified 'plural and conditional' advice**.

29. A related dilemma concerns the presumption, implicit in much evaluation of public engagement, that valuable engagement must produce outcomes that are 'useable' by decision makers. This is often in tension with allowing the freedom to deliberate widely and define key issues independently. Engagement should inform decision making without merely providing ready-made reasoning. We conclude that engagement criteria of 'policy relevance' should not be so narrow that outcomes of public engagement are considered relevant only if they answer policy makers' predefined questions.

30. A fourth dilemma concerns representativeness in public engagement and the relevance given to the views of a small number of participants compared to the vast number of individuals not involved. There are also dilemmas around selection: are the views of a socially representative group, for most of whom the issues are of little interest, more important than a group comprising those with an expressed interest? There are undoubtedly dangers in using samples as a mandate to justify decisions, but there are nevertheless benefits of deliberation and engagement that accrue to policy makers who engage with plural public perspectives.

31. There are further dilemmas that concern asymmetries of power and knowledge: for example, the extent to which public engagement has the effect (consciously or unconsciously) of itself informing the societal perspectives it aims to understand. Another difficulty arises from the obscurity of emerging biotechnologies, which means that 'bottom up' engagement rarely occurs except among already 'engaged' interests with established agendas. Commissioned 'top down' initiatives, however, typically only come about once the issues have been invested with political values. There is no simple or quick solution to raising the level of public engagement and debate concerning biotechnology issues generally. But one implication is that a range of forms and styles of public engagement are likely to be needed, including spontaneous 'uninvited' initiatives that take shape outside planned or institutional structures.

32. We consider how far markets can take the place of public engagement (as a way of signalling preferences) to the extent that both can be seen as ways of aggregating social preferences. We find (notably in Chapters 4 and 9) that while in the case of emerging biotechnologies markets can fail to allocate resources effectively to important social objectives, the value of public engagement in bringing social values into biotechnology policy and governance depends crucially on the quality of the ethical and political discourse.

33. Finally, we consider why biotechnology may be exceptional in requiring public engagement. One possible reason is the remoteness of bodies such as the research councils from traditional channels of democratic accountability. Other reasons include the long timescales involved in both the development of technologies and the realisation of their impacts and the need to enrich the limited treatment of biotechnologies in political institutions.

Research (Chapter 6)

Biotechnology research has a public dimension that entails responsibilities of candour and public reasoning. The participation of researchers in public discourse, for example, as communicators and government advisors requires them to resist pressures to inflate expectations of societal and economic impact, or to gloss over uncertainties and complexities associated with emerging biotechnologies and the innovation system.

34. We examine the role played by researchers in shaping the emergence of biotechnologies, looking both at the influences *of* researchers on the trajectories of biotechnology research, and the influences *on* researchers that govern how their influence is brought to bear. We consider two extreme views: that researchers themselves determine the direction of their research and that researchers are merely instruments in society's attempts to achieve goals through science and technology. We ask how the changing relationship between science and society may rebalance the position of researchers between these two extremes. The search for commercial returns, transnational pressures and convergence between different technologies can make the direction of research itself seem like an emergent property of the research system.

35. We find that it is surprisingly difficult to trace in detail where research in emerging biotechnologies is carried out or how it is funded. This is due, partly, to the lack of agreed terminology and to a failure to identify clearly the nature of research in emerging fields. However, it is clear that alongside universities and institutes established by charities and research councils, relevant research is also carried out by large and small firms (and possibly, also independently of recognised institutions, for example, by 'do-it-yourself' biologists). Likewise the main sources of funding for specific programmes and projects comes from government, directly and via research councils and the Technology Strategy Board, as well as via the European Union, charitable and philanthropic organisations and commercial firms.

36. Commercial firms influence national research policy to the advantage of their sectors or specific businesses, through the construction of powerful visions. We consider the applicability of roadmapping exercises to emerging biotechnologies and conclude that these should be approached with caution. The UK synthetic biotechnology roadmap, which is prudently not a technology roadmap on the model established in more predictable fields of technology, sets down an important marker for the development of responsible innovation in that field.

37. Research in biotechnologies is also strongly shaped by the visions encapsulated in 'grand challenges' and the idea, implicit in the 'biotechnology wager', that biotechnology holds a privileged power to address a range of societal challenges such as food and fuel security. To ensure that the formulation of challenges does not unduly limit social choice we recommend that, **when framing science policy through societal challenges, a 'public ethics' approach should be taken to avoid an overemphasis on technological rather than social solutions to problems with substantial social dimensions**.

38. We find that the expectations placed on researchers are compounded by the 'impact agenda' that has become established in underpinning academic research. We find that this can lead to inflationary cycles of 'overpromising' and 'overbelieving' that risk undermining public trust in science and technology, and misleading national policy, much as they have previously misled commercial investors (see Chapter 9). This is observed particularly in relation to economic impact which is consistently treated as a more direct and immediate outcome of research than evidence suggests is likely. In response to this we recommend that **public systems for the allocation of research funding should be designed to avoid encouraging researchers to overstep the bounds of their competence when assessing the impacts of their research in non-research contexts**.

39. Nevertheless, researchers themselves may exert significant influence through the ways in which they communicate their research to their peers, funders, the media and the public. However, it is easy for their communications to be distorted by popular visions or framed by unrealistic expectations. We have argued that biotechnology research has a public dimension and researchers therefore have public responsibilities. We recommend that **those engaging in public discourse should not only accept responsibility for the factual accuracy and completeness of information they present but also use their best endeavours to ensure, through their continued participation in this discourse, that it is appropriately qualified and interpreted when represented by others**.

40. Researchers have an important role as gatekeepers of knowledge but the main mechanism through which this is exercised, the peer review process, has weaknesses when applied to substantially novel and interdisciplinary research. As public figures, communicating research to a wider audience, and as advisors to governments and funding bodies, researchers have a particular responsibility to exercise self-restraint and vigilance to avoid projecting a false sense of 'scientific certainty'. On the other hand there should be more licence for researchers publicly to advocate research in terms of public good that goes beyond simple economic benefit.

41. There is a particular difficulty for policy makers in identifying sources of technical advice given that judgments about the quality of expertise is itself a matter requiring technical competence. To prevent the premature establishment of orthodoxies in fields characterised by uncertainty we recommend that **in all cases in which technical advice is sought by policy makers there should be a demonstrable attempt to avoid sole reliance on a limited range of established experts in particular fields**. Similarly, the context in which biotechnology research takes place can benefit from more interdisciplinary participation, including between the natural and social sciences, to explore the broader significance of research before disciplinary understandings become entrenched.

Research and Innovation Policy (Chapter 7)

> The emphasis on economic outcomes in research policy detracts from reflection on other important ethical values and is itself founded on insecure assumptions that require more examination. In emerging biotechnologies, policies should foster diversity of technological research while continuing support for innovation should be determined more prominently by social values rather than by market values alone.

42. In this chapter we examine the way in which research policy shapes the emergence of biotechnologies, focusing mainly on the UK and on the twenty-first century. Research policy for emerging biotechnologies does not have a single source and cannot be found in any single

document. The main places in which support for biotechnologies is decided are a small number of pharmaceutical and industrial firms, research councils, medical charities and a large number of dedicated biotechnology firms.

43. Strategic advice to government on the 'big picture' of biotechnology has declined with the winding up of a number of high level bodies created at the beginning of the century, which has reduced opportunities for broad debate and public access. At the same time government technology policy, including in the life sciences, has become increasingly framed by the single dimension of economic growth. While economic benefits are important, they are not solely important, and they risk obscuring other important values, though these are more difficult to quantify. The economic paradigm now dominates policy relevant to emerging biotechnologies in the UK, except the policy of charitable funders who continue to have a substantial role. Areas such as synthetic biology and personalised medicine become a focus for funding by virtue of estimates of the market value that they promise to deliver. Such policies, however, lack relevant evidence in support, although they conform to a number of assumptions that have become commonplace in research policy.

44. Reflections on research policy assume that states should fund research because it is a 'public good' that would be underprovided by the market. However, the real reasons states fund research are more complex, and include national security and economic growth. We find that there is a case for publicly funded research to generate knowledge so that it can be made available to all, independently of private interests, in order to defuse the dangers of 'overpromising' and 'overclaiming' that we have identified.

45. We investigate the assumption that 'Britain is good at research but poor at commercialisation'. We find that Britain is indeed good, but not exceptionally good, at research compared to its major competitors; while on the other hand it has actually been reasonably successful in commercialisation (although this success has declined in recent history). However, there is little evidence to link the relatively strong underpinning research in UK institutions with successful commercialisation by UK companies. Given the transnational organisation of research, and the multinational organisation of the biotechnology industry, only a fraction of research and development feeds into national growth. While there is certainly a need for better economic evidence in this area, we recommend that **the determination of biotechnology policy should attend explicitly to diverse perspectives and bodies of evidence rather than privileging a single, quantitative frame of evaluation (such as economic costs and benefits, or costs and benefits reduced to economic values)**; this should feed in not only to government policy but also to funding bodies and, indeed, to research institutions.

46. Another assumption in the policy literature is that biotechnology is central to social and economic transformation and should be supported, drawing on an implicitly linear model of technical change. However, such assumptions lack the support of reliable correlations between innovation and social and economic outcomes, and fail to take into account the complexity of real-world innovation systems. We find that the difficulties facing the pharmaceutical industry and lack of returns on its investment in biotechnology over thirty years give grounds for greater caution. We recommend that **there is a need for serious evaluation and assessment of past research policies, both of Government as a whole and of particular public funding bodies, to understand in what conditions, if any, selective approaches to support for biotechnology are plausible**. We find that selective approaches in research policy are likely to be fruitful only in very unusual conditions and, as a way of hedging against uncertainty, recommend that **policy makers should consider adopting an approach to social objectives that fosters diversity of research approaches, not just within the particular domains of individual funding bodies but across physical and life sciences, and the social sciences, combined with selective conditions of innovation that involve social benefit rather than just market value**.

47. We examine the assumption that detailed priorities in basic research are set by researchers under a general strategic steer from government (loosely referred to as the 'Haldane principle') and find that the issue of who controls UK research policy is far from clear, although business and industry figures occupy prominent places in the key decision making bodies (advisory bodies such as the Technology Strategy Board, and the research councils). We take note of initiatives to include and even institutionalise broader societal perspectives in research strategy but find there is a persistent asymmetry of influence. We therefore recommend that **research policy should**

be framed not by received assumptions but through continuous engagement with a broad range of societal interests and with the involvement of social actors who can bring understanding of these interests to the joint enterprise of constructing a public frame for research policy decisions.

48. To increase coordination and diversity of government support for research across disciplines, and to encourage the pursuit of public good that is not identified solely with economic performance, we recommend that **consideration should be given to bringing Government research policy and funding bodies under a senior minister (i.e. of Cabinet rank) free from departmental responsibilities to ensure that research properly reflects all the objectives of Government, rather than those of a particular department**. Furthermore, in order to increase openness about the way in which policy relates to social values, we recommend that **there should be a clearly defined, written and published Governmental research policy against which detailed elements of departmental and other public research policies (such as the approach and methods of funding bodies) may be assessed**, and that this should not be produced, as it was formerly, by the Treasury.

Regulation (Chapter 8)

Established regulatory systems may be maladapted to emerging biotechnologies, and the anticipation of downstream regulatory constraints may exert a negative selective pressure on them. Regulating emerging biotechnologies for the public good is not a matter of better regulatory design but requires reflection, engagement and adaptation to mitigate against undesirable crowding out or locking in of biotechnologies.

49. We sketch the main aims of regulation and note that these typically require striking a balance between enabling benefits and managing risks. We note that 'biosafety' and 'biosecurity' are particular concerns within the regulation of biotechnologies. We note that biotechnologies may be particularly susceptible to 'dual use' (i.e. being used for malign as well as benign purposes) in comparison to other technologies, as it is often the conditions of their use rather than any further technical adaptation that renders them potentially harmful. Furthermore, given the characteristic uncertainty associated with emerging biotechnologies and the fact that what constitutes risks and benefits has complex social dimensions (in addition to obvious physical harm), we argue that the focus on narrow conceptions of risk is inappropriate to emerging biotechnologies.

50. We identify a number of tensions within the design of regulatory systems. While biotechnology innovation is global in range, regulatory culture tends to be national in organisation and national in its preoccupations and sensibilities (for example in relation to its attitude to the ethical permissibility of certain practices). However, it has to function in a supranational multilevel system, which creates tensions and problems of accountability and control. Finally, especially in emerging fields, it is often dependent on private institutions and compliance.

51. The regulatory landscape that emerging biotechnologies must negotiate is a patchwork of largely ad hoc institutions. Some are established with statutory functions which makes them inflexible when it comes to accommodating novelty; others, particularly those that have grown out of advisory committees in response to emerging biotechnologies in the past, may have undergone mission creep from advice to regulation, and from scientific to social and ethical advice, but are frequently ill-equipped to provide public-level regulation or to create a site for engagement between a full range of perspectives.

52. The design of regulatory systems faces a number of dilemmas and trade-offs, for example between centralisation of surveillance and localised control; between adequate detail and over-complexity; between faithful administration and responding to evolving social perspectives; between consistency across a broad range of activities and meeting the needs of a specific sector; and between trust and prescriptivism, backed by enforcement.

53. We suggest that the resolution of regulatory dilemmas can be inhibited by over-attachment to certain features and principles of regulatory design, including inappropriate application of the

precautionary principle to the single dimension of risk management, overemphasis on surveillance, over-intrusive regulation and 'soft' regulation. We conclude that regulatory design cannot provide all the answers to securing benefits or averting harms from emerging biotechnologies, not least because emerging biotechnologies do not fit easily into risk-based regulatory models but require instead an approach guided by caution which, in turn, requires a continuous and reflective engagement with broader societal interests.

Commercialisation (Chapter 9)

Markets often fail as effective mechanisms for organising resources in order to fulfil social objectives. In addition to the selection of the most promising and desirable biotechnologies by political, industrial and scientific elites, and leaving commercial competition to determine which innovators and innovations survive in the marketplace, social values can play a role in the shaping and selection of future biotechnologies. One approach could involve the state influencing commercial innovation by directly rewarding the public goods produced by commercial firms in accordance with social priorities determined through public discourse ethics.

54. We review the challenges faced in commercialising emerging biotechnologies, given the peculiarly long development phase and uncertain outcomes associated with them, and consider the effectiveness with which the market mechanism organises resources for biotechnology innovation to produce outcomes of social value.

55. The prospect of gain from biotech 'spin-outs' for academics and their institutions has brought commercial values directly into the publicly-funded research sector. Meanwhile, in the currently most commercialised sector, pharmaceuticals, a disappointing flow of new drugs has merely intensified the pressure on researchers to make their activities profitable. One result of this has been to rely more on academic centres and small specialised firms to carry out the most uncertain work.

56. If the most valuable activity in biotechnology is the production of knowledge, commercialising such knowledge relies substantially on the patent system. This gives the owners of the knowledge the exclusive opportunity to exploit it commercially for a defined term. It is the expectation of profits from this exploitation that provides the main incentive to innovate. We review the use and operation of the patent system for biotechnologies (specifically in the pharmaceutical sector) and find that the patent system has two principal shortcomings. First, the term of patent protection may be too *short* to allow innovators in emerging biotechnologies fully to recover, from their successful products, the costs of developing them (and offsetting the costs of those that failed). Secondly, patents in emerging biotechnologies have a tendency to provide over-*broad* protection, potentially stifling competing research and innovation.

57. Economic analysis of the pharmaceutical sector reveals a further problem with potentially more widespread implications. Patent protection allows an innovator to charge a price well above the marginal cost of production and distribution. But this price will make it inaccessible to many who would benefit, while at the same time failing to capture for the innovator all the potential social value of the product. Biopharmaceuticals, which may offer significant benefits, but only to a limited population of patients, are perhaps most affected. The entry of 'me-too' followers into the market further reduces the profit accruing to the innovator and thus the incentive for radical biopharma innovations.

58. We consider the extent to which the experience of the pharmaceutical industry can be generalised to other biotechnology sectors. We conclude that market failures are most concentrated in highly research-intensive biotechnologies with applications in open biological systems, such as pharmaceuticals and plant breeding. Biomanufacturing technologies (e.g. manufacturing processes for fuels or materials) suffer from a different kind of market failure, namely the under-pricing of alternative incumbent technologies in relation to their true social costs (such as higher greenhouse gas emissions from fossil fuels than biotechnological alternatives).

59. We consider ways of alleviating any restrictive effects of patenting on innovation. These include the use of compulsory licensing, 'open source' licensing, or the designation of research as 'pre-competitive'. Collaborative efforts (including crowdsourcing) also offer strategies to accelerate

research. For example, collaborative validation of potential therapeutic targets for new drugs and the identification of commonly acceptable surrogate endpoints (e.g. using biomarkers) to reduce the time and expense required to satisfy regulatory requirements. Biotechnologies may also benefit from very general incentives such as 'patent box' initiatives (that reward innovation through a reduction on corporation tax for products based on qualifying patents).

60. What none of these approaches achieves, however, is a reward for innovation that is directly linked to the social value of the innovation. Corporate social responsibility measures may play a role in encouraging firms to pursue socially valuable innovation and we recommend that **innovation should be included in corporate social responsibility reports as a separate, specific issue**. The development of QALYs for use in NHS drug purchasing guidance in the UK, and the move to value based pricing of drugs, are measures that are designed to bring price into line with social value. However, the persistence of the price mechanism still requires the innovator to recover their reward for innovation as a multiplication of price by the quantity of the product sold. As a radical alternative, we recommend that **consideration should be given to state interventions in the market for new biotechnologies to secure the social benefits of innovation through direct reward for socially valued innovations**. In particular, further attention should be given to schemes that directly reward the positive social impact of innovation and penalise (via taxation) incumbent technologies that have a negative impact in order to incentivise socially desirable technology change.

61. A specific mechanism for separating the reward for innovation and reward for production is discussed. Under this mechanism the price paid for a product would be set at a sufficient level just to incentivise production. Innovators would then be rewarded separately through an appropriately designed impact payment scheme. We note how, in the UK, health service structures are well suited to the determination of impact in terms of health outcomes; public discourse ethics provides a process through which the social value of these outcomes could be understood.

62. We consider how a social impact approach of this sort could be broadened beyond biomedicine to other biotechnologies that intervene in natural biological systems (for example, to plant breeding) and beyond the UK. We find that, in biomanufacturing, impact payments are unnecessary and inappropriate: here the necessary incentives will be provided by steering of the market mechanism through, for example, ecotaxation. However, here, too, there is a role for public ethics to understand how commercial incentives should be aligned with public good.

Conclusions and recommendations (Chapter 10)

63. The conclusion extracts the main argument that has been developed in the course of the report in support of a 'public ethics' of the kind that is proposed in Chapter 4. The recommendations are then related to the conclusions that are reached in specific contexts and to the virtues that underpin our ethical approach. Thus, whereas this summary has provided an overview of what the reader will find in the report, the conclusion shows where the arguments contained in the report have led.

Introduction: a guide for the reader

What is the aim of this report, in a nutshell?

1. Biotechnologies of many forms present some of the most important sources of transformation and disruption in the world today. The potentialities, uncertainties and ambiguities are enormous, yet the form and directions taken by emerging biotechnologies are not a given, nor are the benefits self-evident. In practice, only a fraction of the technologies that are possible can actually ever be fully realised. As particular developments take place, others are foreclosed; the particular technologies that are prioritised in research and development depend not only on the general societal benefits but also on historical chance and momentum, and the deliberate or inadvertent effects of vested interests and power. Important ethical and political issues are therefore raised, presenting significant challenges for governance. This report will explore these issues and challenges, and make recommendations to guide improved practice in policy making, in research and regulation. The aim is to help maximise the socially beneficial and democratically accountable governance of emerging biotechnologies.

What kind of report is it?

2. This report is not focused on a particular historical development (for example, the ability to synthesise DNA) or even a particular sector (such as medicine, agriculture or industry). Nor is it addressed to a single professional role (research, policy making, business, etc.). Instead it addresses the shaping and selection of emerging biotechnologies (and of technological responses to social challenges more generally) through the way in which decisions and conditions in these various contexts are related. Indeed, it is one of the insights of the report that the segregation of decision contexts and the order in which they are prioritised constitutes a source of potential failure to maximise social value through biotechnologies.

3. Our subject is therefore not emerging biotechnologies as such, but how we think about emerging biotechnologies. The report is intended to stimulate thinking in a variety of different contexts where conditions that influence emerging biotechnologies are set. But it is a stimulus to thinking in a particular way, namely, thinking that is directed outside that immediate context and orientated by the shared interest in promoting the 'public good'. Its recommendations are therefore largely about the processes of reflection and decision making rather than their content. They are guided by a number of procedural and institutional virtues that underlie the 'public ethics' approach set out in the report.

Why does the report focus on 'emerging biotechnologies'?

4. In the report we treat technologies as 'conjunctions of knowledges, practices, products and applications'. Biotechnologies involve biological processes, systems or elements within this conjunction. Despite the great diversity of biotechnologies, the conditions that lead to particular conjunctions coming into being in a particular social and historical context while other possible conjunctions do not, raise common sets of issues. These conditions include both natural constraints and voluntary choices (even if those choices are not always recognised or explicit). Such choices depend on complex judgments involving values, beliefs and expectations about the technologies and their uses. How these choices are made – how different values, beliefs and expectations are drawn in, evaluated, incorporated or excluded – just as much as the nature of the considerations involved, have important ethical and political dimensions. Just as choosing the conditions governing emergence is a common issue for biotechnologies it may be equally common to other, non-biological technologies. Several considerations, however, make biotechnologies a particularly appropriate and timely focus.

5. One is that biotechnologies, broadly defined, concern living systems as opposed to inanimate ones. Although this conceptual distinction has variable significance, there are many perspectives that are relevant to social choice and scientific decision making from which it is important.

6. A second reason is historical. The exploitation of the biological sciences is said to be about fifty years behind the exploitation of the physical sciences. Such comparisons have given rise to some ambitious predictions about the productivity of the biosciences, but they also raise questions about the relative complexity, openness and controllability of the systems with which physical and biological sciences deal.

7. A third reason is connected to the expectations that form around emerging biotechnologies, and the political investments that are placed in them. Biotechnology is held up as an important source of future remedies for current challenges and crises, from food and fuel security to environmentally sustainable production, healthcare and economic growth. It is a significant component in current UK industrial strategy and in advancing the UK as a knowledge economy. It is therefore already a significant social choice.

8. Finally, despite the wide range of questions about technology and social choice, as a bioethics council our interests are necessarily orientated towards the biological, although throughout this report we hold in mind the relationship of biotechnologies to other technological fields and, indeed, to alternative approaches to social objectives.

What is the intended impact of this report?

9. The aim of the report is to cultivate a mode of thinking about and governing emerging biotechnologies that facilitates the balanced engagement between different kinds of norms and values appropriate to the nature of the technologies and the social choices involved, one that properly reflects the public interest in them. This is different from the reflection characteristic of usual ethical assessment of new technologies, which is incorporated as part of a decision process or as a separate initiative associated with major scientific research programmes – for example, in the well-known form of 'ELSI' assessments. In conventional ethical assessments, ethical reflection becomes an additional stage in the process, but one that may be already framed by other sorts of values, circumscribed by its place in the sequence of decisions. The kind of reflection this report intends to cultivate is not conceived as an element of the *process* of decision making in technology policy and governance. Instead, the objective is to cultivate ethical reflection as a characteristic of the *context* in which the process of technological research, development and innovation occurs.

10. The procedural virtues we identify are not, therefore, a matter of 'biotechnology ethics' but of 'public ethics'. A public ethics involves a greater engagement with public values (which means determining values in the public sphere). This is not a novel prescription, but nor is it easy to fulfil – we acknowledge that 'public engagement' initiatives, for example, are fraught with dilemmas. It is not achieved by amending procedures but by altering behaviours, not just by more public engagement, but by engagement that is more 'public' in its nature, engagement that explores public values rather than engagement that expresses private interests.

11. One area in which public ethics can have impact is biotechnology policy. This has traditionally mixed two opposite elements: state intervention, where expert elites decide where to concentrate the resources available for technology development, and market mechanisms that select the technological 'successes' (while other approaches and other businesses are left to founder). Both extremes have limitations that are particularly pronounced with complex technologies and innovation systems, such as are typical of biotechnologies. In simple terms, picking winners is vulnerable to uncertainty and markets may fail to distribute resources to produce greatest social value. To a certain extent the hybrid innovation systems in existence for biotechnologies already represent a middle way, but they remain too 'dirigiste' in their practice and too 'laissez faire' in their values. Bringing public ethics into biotechnology governance is intended to foster a more socially responsible approach to biotechnology governance that introduces social value as a third element in the shaping and selection of the pathway of biotechnology development, alongside elite opinion and market forces.

Who should read this report?

12. The report is addressed to all those who may participate in shaping the emergence of new biotechnologies. This includes those who have formal responsibility for decision making and those who influence or inform decisions, whether as decision makers, advisors, lobbyists, activists or interested non-specialists. Chapters of the report deal with the involvement in governance of researchers, policy makers, regulators, those working in industry and those with no professional involvement (often designated as 'the public'). The report is intended to help each of these to think beyond the decisions that they face within their immediate context and about how their decisions constrain or frame the decisions of others.

13. However, we hope also that the report reaches a wider readership. Although it is not an explicit objective or a likely outcome of the report to stimulate broader interest in the governance of emerging biotechnologies, it is part of the argument of the report that biotechnology governance is improved by a greater level of social engagement with technology choice. We hope that the report may also, therefore, provide a resource for a more engaged public.

Part 1

Understanding emerging biotechnologies

Chapter 1

The biotechnology wager

Chapter 1 - The biotechnology wager

Chapter overview

Biotechnologies are significant in almost every aspect of human welfare and well-being, from medicine, to food and agriculture, fuel, climate change, and the 'knowledge economy'. The frequent presentation of biotechnology in general as fundamental to future well-being and prosperity suggests that a high stake has been placed in its capacity to fulfil these demanding expectations. However, markedly different views can be taken both about the potential of particular biotechnologies to fulfil these expectations and about how their impacts are to be valued. To illustrate this we consider a range of examples of the achievements, shortcomings and potential of biotechnologies in a range of fields.

We characterise the emergence of biotechnologies as the bringing together of knowledge, practices, products and applications. We note that this process does not conform to a consistent model, that it is poorly understood historically and difficult to control in the present. The contingency of this process suggests that it is appropriate to pose questions about the value of biotechnologies in terms of opportunity costs in order to reveal the assumptions and mechanisms of emergence and identify possible sites of control.

We shift perspective from the emergence of biotechnologies to the conditions in which biotechnologies emerge and distinguish a material context of constraints and conditions, and a discursive context of debate and deliberation in which the material conditions are set.

We describe processes by which technologies adapt to their material context, processes that can 'lock in' technological forms and 'crowd out' others. We describe a dilemma of technology control (the 'Collingridge dilemma') in which decisions taken in the absence of evidence can lead to 'locked in' technological forms that may turn out to have undesirable or suboptimal social consequences.

The biotechnology wager

1.1 The future of human well-being has never seemed more entwined with the choices we make about technologies. Throughout modern history, technology has been at the heart of advances in agriculture, medicine and industry that have seen unprecedented growth in global population and rises in life expectancy and standards of living. In the present century, biotechnologies have emerged as a source of potentially transformative innovations. Experience shows that the same technologies that deliver substantial benefits may also bring unintended consequences, both direct (like antibiotic resistance) and indirect (like loss of biodiversity or accentuated inequalities, both within and between nations).[1] Nevertheless, belief in the potential of biotechnologies for endless progress remains powerful, governing substantial financial and political investment. In order for more people to enjoy longer, healthier, richer and more comfortable lives, it is as if we have – collectively – made a wager on the technologies of the future supplying the means continuously to outrun the costs of consumption and growth.

1.2 This 'biotechnology wager' has both a strong and a weak form. In its weak form it amounts to betting on biotechnologies to deliver future benefits of a kind or to a degree that could not be achieved by alternative approaches. Should this bet miscarry, it would represent a setback in terms of wasted resources and foregone opportunities. In its strong form, it embodies the belief that global challenges such as climate change, food and fuel security and pandemic disease, that exist in part because of the global diffusion and success of past technological advances, have 'locked in' a dependency not only on the continuing performance of existing biotechnologies but *on endless progress in biotechnologies* for the preservation even of existing standards of living. This amounts to a wager on biotechnologies providing remedies for the consequences of past and present use of technology while, at the same time, meeting the challenges of ever increasing consumption and novel threats. Such a wager offers a reason to defer action to address current challenges, inequalities and threats in the anticipation of a future technological solution.[2] Whether we accept the necessity of the wager in its strong or weak

[1] European Environment Agency (2001) *Late lessons from early warnings: the precautionary principle 1896-2000*, available at: http://www.eea.europa.eu/publications/environmental_issue_report_2001_22. Unintended consequences may be both good and bad and, indeed, ambiguous. Increasing global food production has supported increasing population, which has led to further pressure on resources.

[2] This point is made strongly by the economist Paul David: "…it may be a functional response on the part of modern industrial democracies to direct the energies of society away from redistributive struggles and towards the cooperative conquest of the 'endless frontier' of science and its commercial exploitation through technological research and development." David PA

forms, or the faith in limitless progress that it represents, will depend on how we view the challenges we currently face and the alternative responses available.

1.3 If the notional 'biotechnology wager' describes our current commitment to advances in biotechnology, we might reasonably ask how such a wager could come to be made. For example, is it a conscious decision of one or more technologically advanced societies, albeit a decision whose consequences may also bind those in other parts of the globalised world? Is it a decision that enjoys a democratic mandate or an arrangement reached between political, industrial and scientific elites? Is it a conscious decision of anyone at all, or simply the cumulative consequence of many uncoordinated acts, the 'invisible hand' of market forces? This question of how the biotechnologies we end up with come to be determined – and of how they should be determined – by whom, and in relation to what values and criteria, is the central question of this report.

Bio-optimism and bio-pessimism

1.4 In all of the fields in which biotechnologies may play a role – climate, food, energy, medicine, and the economy among them – we encounter both utopian and dystopian visions. The emerging field of synthetic biology, for example, has been compared to the 'green revolution' in the mid-20th Century and the 'information revolution' that followed it. Compared to the physical sciences, scientific understanding in the biosciences during the last few decades has achieved a very great deal in a very short time. On the other hand, *useful* biotechnologies have, so far, been much slower to appear and less transformative than public, policy makers and investors may have hoped or expected. External investment has moved away from the sector, business models have been thrown into turmoil and theories of innovation have been re-examined.[3]

1.5 As well as uncertainty about the likely scale (or timescale) of the impacts of prospective biotechnologies, there may also be significant disagreement about the nature and desirability of the impacts. Experience suggests that few benefits are obtained without some cost, and that few achievements are secured without repercussions. This suggests two axes against which attitudes and expectations concerning prospective biotechnologies may be plotted: those of impact (ranging from trivial to transformative) and benefit (beneficial to harmful). As biotechnologies are implemented and diffused, and evidence begins to accumulate, these expectations may be confirmed or confounded and the majority of evaluations may converge on a particular point, although this is by no means necessarily or inevitably the case.

1.6 Ambivalence about prospective biotechnologies may often give way to polarised views when key questions about technology are posed as if what was at stake was a matter of saying 'yes' or 'no' to some fixed idea of technological advance, rather than considering alternative directions for progress.[4] The biotechnology wager, strong or weak, represents a position taken up in one quadrant of a matrix of possible attitudes to prospective biotechnology. However, it is likely that examples of all these attitudes can be found without too much difficulty in relation to almost any prospective biotechnology.

(1991) Computer and dynamo – the modern productivity paradox in a not-too-distant mirror, in *Technology and productivity: the challenge for economic policy* (Paris: OECD), p317.

3 On investment, see Chapter 9. For an assessment of the contribution of biotechnology in the field of pharmaceutical innovation, see: Hopkins MM, Martin PA, Nightingale P, Kraft A and Mahdi S (2007) The myth of the biotech revolution: an assessment of technological, clinical and organisational change *Research Policy* **36**: 566-89.

4 See: Stirling A (2011) From enlightenment to enablement: opening up choices for innovation, in *The innovation for development report 2009-2010*, López-Claros A (Editor) (Basingstoke: Palgrave Macmilan).

Box 1.1: Attitudes to biotechnology

Attitudes towards biotechnologies vary considerably between individuals and over time. Different attitudes may persist in relation to both prospective biotechnologies, and to technologies that are already implemented and well diffused, where evidence relating to them is available. Indeed, attitudes may continue to vary as new evidence and understandings emerge. The examples given below are therefore provisional, and simply suggest where the bulk of opinions appear to converge at the present time.

High impact, Positive net benefit Biotechnologies about which opinion converges in this quadrant are those considered most socially desirable; these may include important 'public goods', for example vaccination.[a]	**Low impact, Positive net benefit** Biotechnologies about which opinion converges in this quadrant may be socially desirable but are more likely to be privately valued (some medicines, for example[b]).
High impact, Negative net benefit Where opinion converges in this quadrant biotechnologies are likely to involve significant public harms or risks. These may not be apparent at an early stage so technologies may be widely implemented before they are recognised. Examples outside biotechnology include chlorofluorocarbons (CFCs) and asbestos.[c]	**Low impact, Negative net benefit** Comparatively poorer performance than alternative; they may tolerated owing to a greater value being placed on the exercise of individual freedom (for example, technologies on the borderline of 'health care'[d]).

[a] The impact and positive benefit of vaccines is well documented.[5] However, although vaccination is generally considered to have a positive net benefit, this is contested by some groups (especially in relation to compulsory vaccination).[6]

[b] Medicines for certain cancers rejected on the basis of cost-effectiveness (such as by the National Institute for Health and Clinical Excellence (NICE) in the UK) might also fall into this category when they are deemed to have too little benefit in comparison to their cost-per-patient – i.e. if life is extended by a marginal amount.[7]

[c] Both CFCs and asbestos, about which the balance of opinion has now moved fairly decisively into this quadrant, were very effective for their intended use but turned out to have extremely harmful and widespread collateral consequences.

[d] It has been suggested that some applications of genetic screening (pre-implantation,[8] preconception,[9] personal genetic profiling[10]) may, under some perspectives have negative benefit (raising anxieties unnecessarily, involving medical procedures with no clear benefit, giving false confidence, causing unnecessary pressure on public health services, etc.). However, there is usually sufficient ambiguity about the harms that the infringement of personal and commercial freedom that would be involved in banning those technologies argues against prohibiting them. This tolerance may be important – it is worth recalling that the balance of views about many 'disruptive' technologies may be initially fall into this quadrant.

The biotechnology balance sheet

1.7 Examples of genuinely harmful technological impacts from the past should be hard to find as markets, governance and regulation should weed them out before significant harmful effects accumulate. However, it may take some time before undesirable effects are recognised and

[5] "The impact of vaccination on the health of the world's people's is hard to exaggerate. With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction or population growth." Plotkin SL and Plotkin SA (2004) A short history of vaccination, in *Vaccines*, Plotkin SA Orenstein WA and Offit PA (Editor) (China: Saunders Elsevier), p1. See also: Payette P and Davis H (2001) History of vaccines and positioning of current trends *Current Drug Targets - Infectious Disorders* **1**: 241-7.

[6] For a discussion of attitudes to vaccines and vaccination programmes, see: Larson HJ, Cooper LZ, Eskola J, Katz SL and Ratzan S (2011) Addressing the vaccine confidence gap *The Lancet* **38**: 526-35.

[7] See, for example, the situation in the UK with regard to the drug everolimus: NICE (2012) *Everolimus for the second-line treatment of advanced renal cell carcinoma*, available at: http://publications.nice.org.uk/everolimus-for-the-second-line-treatment-of-advanced-renal-cell-carcinoma-ta219, and BBC Online (2011) *NICE rejects kidney cancer drug everolimus*, available at: http://www.bbc.co.uk/news/health-13115961.

[8] Brown R and Harper J (2012) The clinical benefit and safety of current and future assisted reproductive technology *Reproductive Biomedicine Online* **25**: 108-17.

[9] Human Genetics Commission (2011) *Increasing options, informing choice: a report on preconception genetic testing and screening*, available at: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/Increasing%20options,%20informing%20choice%20-%20final.pdf.

[10] The issue of genetic profiling has also been subject to considerable and recent debate. See, for example, Nuffield Council on Bioethics (2010) *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, available at: http://www.nuffieldbioethics.org/personalised-healthcare-0; Human Genetics Commission (2003) *Genes direct*, available at: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/genesdirect_full.pdf and Human Genetics Commission (2007) *More genes direct*, available at: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/More%20Genes%20Direct%20-%20final.pdf.

begin to tip the balance in favour of modified or alternative technologies (or stimulate the search for alternatives). In framing the question of how technologies come to be developed and brought into use it is instructive to consider how existing technologies may accumulate undesirable side-effects and how the beneficial and unwanted effects are distributed. To assess the impetus behind the biotechnology wager, it will help to understand the extent to which further technological 'fixes' are necessitated by prior use of earlier technologies. We cannot explore this question in detail in every field of biotechnology but we will now consider some examples of the achievements, collateral effects and current possibilities of biotechnology that suggest a level of commitment to the biotechnology wager.

Food security

1.8 A range of technologies, including chemical pesticides, fertilisers, irrigation and plant breeding, have transformed agricultural food production since the 1940s, in particular through technology transfer to developing countries (the 'green revolution'). Artificially bred high-yielding varieties of wheat, rice and maize have been central to this revolution. A more than doubling of global food production in the past 40 years has been achieved despite only an eight per cent increase in the use of land for agriculture in the same period.[11] However, the long term sustainability and social impacts of production methods have come increasingly into question. The very technologies that have made historic productivity increases possible (for example, the Haber-Bosch process to 'fix' nitrogen – converting atmospheric nitrogen to ammonia – for fertiliser) have been accompanied by an accumulation of undesirable collateral effects such as increases in water and air pollution, rising greenhouse gas levels, and the reduction of biodiversity.[12] At the same time, the dependency on fixed nitrogen has been substantially 'locked in' by the need to feed rising populations (particularly populations dependent on some of the least productive land).[13] Biotechnology offers potential responses through the possibility of genetically engineering food crops to increase yield and adapt to new or altered environments, the use of advanced genetics to enhance conventional breeding systems without direct manipulation of the genome, or the development of new synthetic biology technologies to enable the 'designing in' of multiple genetic traits (higher yields, drought and disease tolerance).[14] However, biotechnology is only one element of a potential response to global food security. As such, it must be assessed alongside a range of different scientific, institutional and organisational innovations (like changing the crops under cultivation, 'open source' supply chains, ecological farming practices and support for participatory farmer-led plant breeding).[15]

Energy security

1.9 Demand for energy is predicted to rise by a third between 2010 and 2035, a demand that cannot be met by climate-damaging carbon-intensive technologies if there is to be any prospect of limiting global warming.[16] While the most important contribution to reaching energy security and climate goals is reduced consumption, energy efficient and low emission technology are

---

[11] Beddington J (2009) *Food, energy, water and the climate: a perfect storm of global events?*, available at: http://www.bis.gov.uk/assets/goscience/docs/p/perfect-storm-paper.pdf, citing Parry ML, Canziani OF, Palutikof JP, van der Linden PJ and Hanson CE (Editors) (2007) *Climate change 2007: impacts, adaptation, and vulnerability* (Cambridge: Cambridge University Press).

[12] Erisman JW, Sutton MA, Galloway J, Klimont Z and Winiwarter W (2008) How a century of ammonia synthesis changed the world *Nature Geoscience* **1**: 636-9.

[13] Galloway JN and Cowling EB (2002) Reactive nitrogen and the world: 200 years of change *AMBIO: A Journal of the Human Environment* **31**: 64-71.

[14] The Royal Academy of Engineering (2009) *Synthetic biology: scope, applications, and implications* available at: http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf.

[15] Leach M, Scoones I and Stirling A (Editors) (2010) *Dynamic sustainabilities: technology, environment, social justice* (London: Earthscan).

[16] See: International Energy Agency (2011) *World energy outlook 2011: executive summary*, available at: http://www.iea.org/Textbase/npsum/weo2011sum.pdf. The figure for the rise in demand for energy is based on 1.7 billion population growth and 3.5 per cent global average gross domestic product (GDP) growth over the period, although acknowledging the global economic situation, they estimate that lower short term growth will have only a marginal effect. New approaches are required because four-fifths of energy related carbon dioxide emissions permissible by 2035 (to hit the 2˚C global temperature increase target) are already accounted for by existing infrastructure.

inevitably called for. Biotechnologies may contribute to this in a number of important ways. As all of the projected net increase in demand for oil is accounted for by personal mobility and freight in emerging economies, the engineering of new generations of biofuels that avoid the harmful impacts on land use characteristic of 'first generation' biofuels is strongly favoured, although the technological means by which this could be achieved is currently uncertain.[17] Perhaps the most important contribution of biotechnologies, however, may lie in their capacity to help to make production processes in a variety of applications, significantly less energy intensive.[18]

Biomedicine

1.10 Advances in biomedicine contributed – alongside improved sanitation, nutrition and living and working conditions – to a steady rise in life expectancy and general standards of physical well-being throughout the 20th Century in industrialised countries.[19] Successes in preventing and treating communicable diseases have, in developed economies, shifted the focus onto non-transmissible diseases, diseases of lifestyle and old age, obesity, cancer, heart disease and dementia. While advances over the last century, such as antibiotics, have meant that previously life-threatening infections are now routinely survivable, widespread use of antibiotics in human and veterinary medicine, and in routine livestock production, has been identified as a significant cause in the rise of antibiotic and multi-drug resistant bacteria.[20] At the same time, further challenges have arisen through the resurgence of malaria,[21] pandemic strains of influenza, and HIV. Biotechnologies offer some important strategies to address all these challenges, although in some cases they face substantial institutional, economic and regulatory hurdles, in addition to biological complexity. For example, the realisation of more 'personalised' medicine is far from straightforward not least because a key element, the pharmaceutical industry, is currently struggling to find a business model that would support such a transformation in medicine.[22] Furthermore, it remains the case that market incentives appear to foster greater attention to disorders of most concern among rich populations, than to treating many severe conditions suffered by the global poor.[23]

The economy

1.11 High expectations are placed on bioscience and biotechnology as a major contributor to the economy.[24] The financial crisis that began in the United States and Western Europe in 2007-8, and the subsequent recession, has focused attention on the search for potential new drivers of economic growth. Both the UK and EU responses to the crisis stress the importance of research and development.[25] However, how to translate national investment in research and

---

17 Nuffield Council on Bioethics (2011) *Biofuels: ethical issues*, available at: http://www.nuffieldbioethics.org/biofuels-0.

18 See, for example, the use (and modification) of particular enzymes in the commercial-scale production of some antibiotics and 'advanced' biofuels: Davidson S (2008) Sustainable bioenergy: genomics and biofuels development *Nature Education* **1**; DSM (1999) *DSM to invest NLG 15 million in enzyme plant in Delft (Netherlands)*, available at: http://www3.dsm.com/newsarchive/1999/~en/g_246end31_en.htm. See also: OECD (2011) *Industrial biotechnology and climate change: opportunities and challenges*, available at: http://www.oecd.org/sti/biotechnologypolicies/49024032.pdf, p19.

19 See: Riley JC (2001) *Rising life expectancy: a global history* (Cambridge: Cambridge University Press), p51ff.

20 Russell E (2011) *Evolutionary history: uniting history and biology to understand life on Earth* (Cambridge: Cambridge University Press).

21 Malaria Foundation International (2012) *Resurgence of malaria*, available at: http://www.malaria.org/index.php?option=com_content&task=view&id=130&Itemid=32.

22 In the meantime, some of the challenges of global scope (e.g. malaria) are being addressed by new non-commercial initiatives such as that of the Bill and Melinda Gates Foundation. See: PATH Malaria Vaccine Initiative (2012) *About us*, available at: http://www.malariavaccine.org/about-overview.php.

23 For example, Médecins Sans Frontières and the 'Drugs for Neglected Diseases Initiative' have noted that, out of 1,556 medicines developed between 1975 and 2004, only 18 (21, if malaria and tuberculosis are included) were indicated for diseases that mainly affect people in developing countries. See: Chirac P and Torreele E (2006) Global framework on essential health R&D *The Lancet* **367**: 1560-1.

24 See: Department for Business, Innovation and Skills (2011) *Strategy for UK life sciences*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences, where it is stated, for example that "[l]ife sciences will continue to be vibrant in the UK and will be a *key contributor to sustained economic growth*.", p6. (Emphasis in original.)

25 The second EU 2020 target (part of the EU's growth strategy for the second decade of the new millennium) states that three per cent of EU GDP (public and private combined) is to be invested in R&D/innovation (see: European Commission (2011) *Europe 2020 targets*, available at: http://ec.europa.eu/europe2020/targets/eu-targets/index_en.htm) This is strikingly

development into safe, desirable, beneficial and profitable products that will primarily benefit that nation is perhaps the single most disputable aspect of research policy. Historically, the fastest growing economies have not been high-income countries with high expenditure in research and development but middle-income countries that are able to grow quickly as a result of imitating the technologies developed elsewhere.[26] Furthermore, even where there appears to be a strong relationship between growth and advanced technology, the pursuit of growth does not address the question of the appropriate aims and orientation for technological progress in any particular sector.[27]

1.12 These examples from different fields show that the path of biotechnology innovation is complex, lengthy, difficult to control and subject to unanticipated consequences. In the following sections we consider what distinguishes the emergence of biotechnologies from the delivery of new products or services, namely, the dynamic relationship between the emerging technology and the conditions of its development and innovation.

Emerging

1.13 The term 'biotechnology' is commonly used, but not always well defined. When we refer to 'a biotechnology' in this report we mean a productive conjunction of knowledge, practices, products and applications. 'Practices' in this sense include both techniques that depend on machinery or automated procedures as well as voluntary human actions ('standard operating procedures'). 'Products' include services and consumables as well as tangible and durable objects; these may be intermediate products, for example, machines to be used in production. If a biotechnology is a conjunction of this kind, then in a very simple sense 'emerging' is the *assembling* of this conjunction.[28] Assembling in this sense is always subject to conditions and externalities that both affect it and that it affects. In examining how biotechnologies emerge, we are primarily concerned with the interplay between the potentialities and limitations inherent in the technology, and the conditions that lead to or obstruct the innovation of that technology in a particular place and at a particular moment in history.

1.14 This assembling, or emergence, does not necessarily follow an ordered and linear path from 'science', through applied research and innovation to widespread use, or perhaps may do so only in unusually controlled conditions. The path of emergence may begin at almost any point and rarely runs straight. Some of the most ambitious initiatives in emerging biotechnologies, such as 'BioBricks'® in synthetic biology[29] and the 'virtual patient' in personalised medicine, for example, were driven by applications-focused engineering and information technology initiatives (respectively) rather than by research in biological science. Equally, the assembling does not necessarily require the injection of new knowledge: 'emerging biotechnologies' may emerge as the result of a convergence between well understood pre-existing techniques that may only become possible when certain external conditions fall into place. This is to say that the emergence of a biotechnology:

- engages different social actors and groups in unique configurations (scientists, engineers, policy makers, publics, etc.);

conspicuous as the only 'input target' out of the five targets (the four others being outcome targets). UK spending was 1.86 per cent GERD in 2009 (see: European Commission (2012) *Europe 2020 in the United Kingdom*, available at: http://ec.europa.eu/europe2020/europe-2020-in-your-country/united-kingdom/index_en.htm).

[26] Edgerton D (2008) *The shock of the old* (London: Profile); see also Chapter 7.

[27] Stirling A (2009) *Innovation, sustainability and development: a new manifesto – direction, distribution and diversity! Pluralising progress in innovation, sustainability and development*, available at: http://anewmanifesto.org/wp-content/uploads/stirling-paper-32.pdf.

[28] In our view, this description as an 'assembling' captures better than 'emerging' the active endeavour involved both in developing biotechnologies and in establishing the conditions that facilitate and govern such development, but we retain the established term to avoid confusion.

[29] See paragraph 2.19.

- is orientated towards solving problems and delivering concrete applications (but capable of capitalising on serendipities);
- draws on knowledge and technical expertise from a variety of fields (producing *ad hoc* productive configurations); and
- is influenced by social, as well as technical, conditions and implications.[30]

1.15 Looking back at innovations of the past, it is easy not to recognise the contingency of the technological pathways that have led to the present.[31] Our understanding of where, why and how novelties emerge is often strongly affected by theoretical models that fail to reflect the great diversity, uncertainty and serendipity of novelty generation.[32] These processes are inherently hard to research. Our understanding of them is limited in that most ideas are not developed and most inventions not exploited. More importantly, by focusing only on how technologies fulfil the expectations that are set for them, we may fail to take account of the unexpected consequences, beneficial or harmful, to which they can lead.

Opportunity costs and counterfactuals

1.16 Stepping back from the narrow focus on biotechnologies to look more roundly at the states of affairs that they address brings into view reasons to hesitate in making the 'biotechnology wager'. One of these is that the focus on 'high' technologies might entrench the values of consumerism and exacerbate inequalities in the distribution of benefits and costs. (Consideration might be given instead, for example, to investing greater political attention and economic support in forms of social and organisational innovation that prioritise the needs of the poorest and most vulnerable people.) While emerging biotechnologies may offer significant responses to current and future challenges in a number of sectors, this question of appropriate mix – both among different biotechnological strategies and between biotechnologies and alternative strategies – is an important but under-discussed one for public policy.

1.17 This broader perspective suggests that the current landscape of technologies is not the only one possible.[33] At earlier points in history, but for the particular conjunction of conditions that obtained at the time, other technologies might have developed that could have led to a very different state of affairs in the present.[34] While such reflection cannot tell us what an alternative, 'counterfactual' present might be like had a different path been taken at some significant crossroads in the past, it serves as a reminder that the present is contingent upon a mixture of past conditions and choices. In a similar way, the future is contingent upon a complex set of conditions that are determined or accepted now. This is not to say that these choices or their significance can always readily be seen in advance; but the choices are likely to be unduly restricted if the way we think about emerging biotechnologies is limited to, or framed as, discrete considerations of specific technologies or specific outcomes. Indeed, an overemphasis on

---

[30] This mirrors analyses of the more complex ways in which knowledge itself may be produced; see: Gibbons M, Limoges C, Nowotny H *et al.* (1994) *The new production of knowledge: the dynamics of science and research in contemporary societies* (London: Sage) and Nowotny H, Scott P and Gibbons M (2001) *Re-thinking science: knowledge and the public in an age of uncertainty* (Cambridge: Polity Press).

[31] Deuten and Rip examine how recollection applies a *post-hoc* rationalisation to explain the outcomes that actually transpired, in the process, marginalising the contingency and precariousness of the process that led to them: Deuten JJ and Rip A (2000) Narrative infrastructure in product creation processes *Organization* **7**: 69-93.

[32] Edgerton has argued that most histories of technology are actually poor guides to what might happen in the future because they fail to identify what were actually the most important technologies in particular periods, or identify them at all, focusing instead on what was considered most novel, controversial or revolutionary. For example, perhaps one of the greatest transformations in human history, namely the massive increase in land and labour productivity in agriculture in rich countries after 1945 is surprisingly absent from general texts on the period, which instead identify the period with nuclear power, rockets, etc. See: Edgerton D (2008) *The shock of the old* (London: Profile).

[33] Ibid. For a discussion of 'counterfactual history' more generally, see: Bunzl M (2004) Counterfactual history: a user's guide *The American Historical Review* **109**: 845-58.

[34] See, for example, the emphasis on the development (and subsequent dominance, in some quarters) of light-water nuclear reactors as a consequence of prevailing military priorities in the US following the Second World War. See: Cowan R (1990) Nuclear power reactors: a study in technological lock-in *The Journal of Economic History* **50**: 541-67. See also the focus on the possibility that thorium fuel cycle reactors offer an alternative: Galperin A, Reichert P and Radkowsky A (1997) Thorium fuel for light water reactors—reducing proliferation potential of nuclear power fuel cycle *Science & Global Security* **6**: 265-90.

specific technologies, 'golden opportunities' or, 'royal roads', for example, risks making any resistance to specific technological commitments appear to betoken an 'anti-science' or 'anti-technology' prejudice. In fact, resistance to innovation is indispensable, and criticism of novelties valuable, in revealing the diversity of options available and the viability of those alternatives.[35]

1.18 The question of 'opportunity cost', of what is foregone in the attempt to secure a selected benefit, is one that is familiar to economists but too seldom adequately considered in relation to technological commitments. Such consideration may appear difficult because it is usually taken to mean speculating about a range of futures where both the possibility of realising them and the values attached to the realisation are so uncertain. It can, nevertheless, provoke a constructive examination of the conditions that constrain decision making, help to illuminate unquestioned assumptions, and identify a broader range of choices that are available. We therefore make the recommendation – one that has guided our own deliberations – that **commitments to particular technological pathways should be evaluated not only in terms of their expected future impacts but also by comparison to possible alternative pathways; this can help to illuminate obscured assumptions, constraints and mechanisms of the innovation system, and help to identify sites and opportunities for more constructive governance, prioritisation and control**. Guided by this recommendation we now turn our attention to the contextual conditions within which biotechnologies emerge and the role that those conditions play in constraining or opening up possible trajectories of development.

Contingency and its consequences

Material and discursive contexts

1.19 We have seen that the emergence of new biotechnologies may be characterised as a contingent, branching process whereby some possible trajectories are selected in preference to others. Different pathways may be explored simultaneously, although probably not all of those that are possible; sometimes a single approach becomes dominant and others are neglected (although they may be returned to later, especially if conditions change).

1.20 The unfolding of this process is governed by a mixture of intrinsic potentialities and contingent conditions. Intrinsic potentialities will include things like hard physical constraints that limit the viability of a given technology and define its operational parameters. Contingent conditions will include things like institutional structures, networks of communication for the transfer of knowledge between researchers, inputs of funding and investment, allocation of resources, legal constraints and regulatory requirements. Together, these intrinsic and contingent conditions make up what we will call the 'material context' of biotechnology emergence.

1.21 While intrinsic potentialities are a given (even if they are not wholly understood), contingent conditions often fall within the scope of human choice, even if they are not actively chosen. Choices may weave together complex moral and factual judgments as well as subtle attitudes and beliefs, values and dispositions. The context in which these are expressed is a 'discursive context' of discussion, debate and deliberation. Such contexts involve different groups of individuals invested with different kinds of powers. The discursive context provides an opportunity to examine hypothetical or imaginary states of affairs and the values associated with them. However, it is also where decisions are made that alter the material context, for example, decisions to initiate a line of research, allocate funding, and impose legal or other constraints. (How the discursive context itself may come to be structured for particular biotechnology decisions is an important question for this Report that we will address in the next Chapter.)

[35] Edgerton D (2008) *The shock of the old* (London: Profile), p9. Such resistance may even be essential and, whereas it is often left to non-scientists and for this reason risks being politically marginalised, is something that scientists themselves should undertake; see: Edgerton D (2011) In praise of Luddism *Nature* **471**: 27-9.

1.22 The selection of contingent conditions can be highly decisive, particularly where there is significant uncertainty about the technology's potential to deliver effective applications. One might think here of the reasons that different approaches to human stem cell research were pursued in the UK, where research has concentrated on licensed use of human embryonic stem cells (hESC), and in Germany, where destructive human embryo research is unlawful.[36]

1.23 Contingent conditions need not be 'all or nothing': they can exert selective pressures that simply favour or deter, to varying degrees, certain pathways in relation to possible alternatives.[37] Their effects are likely to be aggregate, and within this aggregate, one condition may counteract another. Being multiple, they are often determined by a range of different actors (firms, governments, researchers and others) rather than being controlled by a single, well-informed actor following a consistent strategy. These different actors (or networks or groups of actors) will sometimes have significantly different objectives, and different beliefs and understandings of the technological options. A lack of coordination – or outright opposition – can create strong and sometimes counterproductive pressures.[38] Some important conditions may not therefore be the result of active 'decisions' at all, either because they are not the intentional outcome of a single decision (but the unintended consequences of a set of discrete interventions taken without a view to their collective effect) or because they are the result of omissions.[39]

Technological 'lock-in'

1.24 Although some decisions in the global pathway of technology development may be contingent upon sometimes very minor influences, once a pathway is established, technologies can easily become entrenched or 'locked in'. Central to the explanation of technological 'lock-in' is the idea that specific technological pathways, once embarked upon, become progressively difficult and costly to escape. In economic terms, this is generally attributed to the mutual adaptation of the technology itself and market conditions, learning effects and increasing returns to scale, etc.[40] Technologies may also acquire 'momentum' from the feedback between technology and society through, for example, lifestyle adaptations to particular products.[41]

1.25 The adaptations and accommodations that 'lock-in' technologies also, of course, bring gains in terms of efficiency and utility. However, this may mean that the innovation conditions faced by new technologies are most likely to be conservative, since it is probable that they will have been aligned so as to make the most effective use of incumbent technologies. Even where – rather than competing with existing technologies, new technologies open up an entirely new market or

---

[36] Research in the UK has focused primarily on deriving hESC subject to the Human Fertilisation and Embryology Act 1990 (as amended); in Germany, owing to the interpretation of constitutional prohibitions in the Basic Law (Grundgesetz) and s.2 of the Embryo Protection Act 1991 (Embryonenschutzgesetz) it has focused on imported lines (pursuant to the Stem Cell Act 2002 (Stammzellgesetz) (as amended)), somatic stem cells and induced pluripotent stem (iPS) cells. Notwithstanding the permissive legal environment in the UK, research may nevertheless come to be affected by the possibilities of patenting, and therefore successfully commercialising, products in the light of the European Court of Justice's finding in *Brüstle v. Greenpeace eV* (Case C-34/10), 18 October 2011.

[37] For example, tax incentives might be used to encourage particular activities in specific places: scientific and technological endeavour generally might be encouraged (as under the UK Government's research and development relief for corporation tax) or specific disciplines might be given favourable terms (such as New York City's biotechnology tax credit). See: HMRC (2012) *Research and development (R&D) relief for corporation tax*, available at: http://www.hmrc.gov.uk/ct/forms-rates/claims/randd.htm; NYC Government (2012) *Answers to the most frequently asked questions about biotechnology credit against the general corporation tax and the unincorporated business tax*, available at: http://www.nyc.gov/html/dof/html/pdf/10pdf/biotech_faq.pdf.

[38] See paragraph 7.11 below, for an example whereby government investment intended to leverage private sector R&D investment apparently had the opposite effect.

[39] For example, human reproductive cloning research was allegedly pursued for some time in Italy, owing to that country's reticence in legislating for reproductive technologies; see: BioNews (2004) *Antinori restates clone claims*, available at: http://www.bionews.org.uk/page_11939.asp.

[40] See: Boas TC (2007) Conceptualizing continuity and change: the composite-standard model of path dependence *Journal of Theoretical Politics* **19**: 33–54).

[41] The theory of 'technological momentum' was developed by Thomas Hughes in the late 1960s. See: Hughes TP (1969) Technological momentum in history: hydrogenation in Germany 1898-1933 *Past & Present* **44**: 106-32.

range of possibilities – they may still suffer disadvantage through a lack of conducive environmental conditions.[42]

1.26 Conditions in the innovation environment may even ensure that there may only be space for one technological 'winner' that may come to dominate a field of practice to the extent that potential alternatives are 'crowded out'.[43] This winner, however, need not be the 'best' overall candidate from all perspectives,[44] if successive rounds of selection operate according to different criteria (technical, political, social, economic, etc.).

An innovation dilemma

1.27 A dilemma facing a society that seeks to govern innovation is that often the consequences of introducing new technologies can only be fully understood once the technology is in use; by that time, however, it may be too late to change course. This difficulty was expressed by the British social philosopher David Collingridge in the form of a 'technology control dilemma'.

Box 1.2: Collingridge's technology control dilemma

Efforts to control technology face the following dilemma:

1 Limited predictability: "understanding of the interactions between technology and society is so poor that the harmful social consequences of the fully developed technology cannot be predicted with sufficient confidence to justify the imposition of controls."

2 Limited power: "by the time a technology is sufficiently well developed and diffused for its unwanted social consequences to become apparent, it is no longer easily controlled. Control may still be possible, to some degree but it has become very difficult, expensive and slow."[45]

1.28 As presented, the dilemma focuses on avoiding undesirable but unforeseen social consequences of technology, but it might equally apply to the problem of securing the most desirable benefits. The power of the dilemma arises from the fact that the consequences of decisions about what technological trajectories to pursue potentially 'lock in' a given technology and simultaneously 'crowd out' alternatives in a context in which switching paths may set back the achievement of a benefit by decades.[46] Of course, biotechnology innovation has its own special features that are different from the military and industrial technologies considered by Collingridge but the essential point about the need to make commitments in the absence of relevant evidence remains pertinent.

1.29 It is important not to overstate the implications of the Collingridge dilemma. It does not imply that rigorous social appraisal of alternative technological trajectories is impossible at an early stage. (Collingridge's own argument explicitly highlighted the need for greater efforts in this direction.) It does, however, serve to emphasise the sobering predictive challenges that accompany

[42] This may account for the 'productivity paradox' when computers first became widely available, i.e. the seeming disconnection between advances in computing power (and implementation of computing power) and the concurrent slow growth in productivity. (See: David PA (1989) Computer and dynamo – the modern productivity paradox in a not-too-distant mirror, in *Technology and productivity: the challenge for economic policy* OECD (Editor) (Paris: OECD, 1991)). As we suggest in Chapter 8, the absence of a regulatory system for novel biotechnologies does not necessarily give them an advantage over regulated technologies, and adapting an existing system can be difficult.

[43] However, potential alternatives need not always be entirely 'crowded out', as evidenced by the example of electricity generation. Here, strategic vision can deliberately act *against* technically or economically dominant technologies crowding out alternatives. See: Stirling A (2010) Multicriteria diversity analysis: a novel heuristic framework for appraising energy portfolios *Energy Policy* **38**: 1622-34. For a biotechnological example, one might consider the use of 'primer walking' and 'shotgun' DNA sequencing (two techniques used concurrently for (broadly) the same purposes, which are now being replaced with 'next generation' high-throughput sequencing.)

[44] There is some dispute in the economics literature about how far the concept of lock-in can explain apparent market failure to select the best alternative. See, for example: Liebowitz S and Margolis SE (2010) *The troubled path of the lock-in movement*, available at: http://ssrn.com/abstract=1698486.

[45] Collingridge D (1980) *The social control of technology* (Milton Keynes: The Open University Press), pp17-8.

[46] "What happens is that society and the rest of its technology gradually adjust to the new technology, so that when it is fully developed any major change in the new technology requires changes in many other technologies and social and economic institutions, making its control very disruptive and expensive". Ibid.

genuinely novel technologies and urges greater caution, responsibility and accountability in policy decisions about such technologies. It also places a premium on effective social and institutional learning. In particular, there is nothing about Collingridge's important insight into the difficulties of acting with incomplete knowledge that prevents scrutiny of the aims and interests that animate research, development and innovation of emerging biotechnologies.[47] Ignorance of the future means that the problems of absence of evidence may be inescapable, but this also provides the basis of a case for making the governance of emerging biotechnologies more reflective.[48]

Path dependency

1.30 The choices that face a society about what technologies to pursue are rarely as stark as the technology control dilemma suggests. For example, they are seldom about whether to say 'yes' or 'no' to a given technology or, if they are, they are perhaps already coming too late to allow a balanced, unconstrained decision to be made. The decision has been brought to this point, implicitly, because alternatives are already weeded out: the dilemma, if not the technology itself, is already locked in. To engage in a balanced appraisal of opportunity costs it is therefore necessary to consider how the point may be arrived at where this dilemma appears to have become inescapable.

1.31 Sunk costs and market conditions are not the only conditions determining emerging biotechnology trajectories, and perhaps not the most important. Well before the point of innovation, a variety of conditions influence research and development. These conditions include allocation of funding, disciplinary hierarchies and agendas, and research regulation as well as anticipated market response. But the constraints extend also into the discursive context, with intellectual constraints operating as blinkers at critical decision stages. Alternative technological pathways may even be difficult to conceive of because knowledge cultures or certain ways of working can limit the ability to imagine a radical alternative.[49] Even where alternative approaches *can* be conceived, they may be strongly associated with visions of alternative future states of affairs that people will value differently. Therefore the way in which different sets of social, institutional and technological conditions are seen as aligning with these envisaged futures means that certain alternatives may be 'crowded out' at an early stage.

1.32 The fact that the conditions that shape emerging biotechnologies may be determined discretely, in different contexts, and in an ordered sequence implicitly creates 'path dependencies', where prior decisions constrain and condition the range of possibilities available at subsequent stages. The order in which these decisions occur, and the groups to which they are reserved, therefore matter importantly, since earlier decisions 'frame' the subsequent questions. Furthermore, the segregation of different decisions into different technical 'types' to be dealt with by different expert groups prevents broader engagement between these technical domains and means that, because of the ordering, priorities and interests of certain technical elites (scientific, political, industrial) may constrain the effect of other influences. Hence the familiar complaint that ethical reflection is restricted to the conduct and implications of a particular type of research or innovation (i.e. after the scope and nature of the research has been determined) rather than the

[47] For an examination of scrutiny of these areas under conditions of uncertainty, see: Wilsdon J and Willis R (2004) *See-through science: why public engagement needs to move upstream*, available at: http://www.demos.co.uk/files/Seethroughsciencefinal.pdf?1240939425; Scoones I, Wynne B and Leach M (Editors) (2005) *Science and citizens: globalization and the challenge of engagement (claiming citizenship)* (London: Zed Books).

[48] Stirling A (2008) Science, precaution, and the politics of technological risk: converging implications in evolutionary and social scientific perspectives *Annals of the New York Academy of Sciences* **1128**: 95-110.

[49] See, for example, Dosi's work on the concept of 'technological paradigms'. Dosi draws explicit parallels between his idea of a technological paradigm and Kuhn's concept of scientific paradigms. He notes: "'Technology' [in the view of the framework outlined] includes the 'perception' of a limited set of possible technological alternatives and of notional future developments… a technological paradigm…embodies strong prescriptions on the directions of technical change to pursue and those to neglect… certain specific technologies emerg[e], with their own "solutions" to those problems and the exclusion of other notionally possible ones." Dosi G (1982) Technological paradigms and technological trajectories: a suggested interpretation of the determinants and directions of technical change *Research Policy* **11**: 147-62.

question of whether such research or innovation is appropriate in the first place, particularly in the context of other uses of resources.[50]

1.33 This determination of technological paths through managed decision making in technically defined contexts (where certain sorts of technical expertise are privileged) may therefore reinforce path dependency and make consideration of opportunity costs more difficult. Nevertheless, *just because* segregating and sequencing decision stages in this way can create managed path dependency, it offers an attractive approach to governing the emergence of biotechnologies. As a prescription for technology control it raises two sorts of objections, though. The first, as suggested above, is that it offers the possibility of control at the expense of a domination by technical forms of expertise; the second is that, in practice, the way biotechnologies actually emerge is less amenable to such disciplining in any case. In particular, the idea that technical questions can be separated from political questions, and these from social and ethical questions, and that each can be dealt with independently is, we will argue, difficult and potentially misleading to apply in practice.

Conclusion

1.34 In this first Chapter, we have drawn attention to the possibility of ambivalence about biotechnology and some of the vicissitudes of its relatively short history. We have suggested that, at both a local and global level, societies are implicitly committed to securing further advances in biotechnology (the 'biotechnology wager'), either through substantial investment of resources that have significant opportunity costs or, more radically, through the urgent need to mitigate present patterns of growth and consumption in order to avoid catastrophic threats to their welfare. We then suggested that commitments to biotechnology are seldom adequately considered in relation to questions of social opportunity cost but that considering them in this way is a helpful approach to understanding their *social value*. We suggest that the segregation, arrogation and sequencing of biotechnology governance contribute to path dependency that makes balanced governance difficult.

1.35 Our intention in this Report is to draw lessons from the introduction (or obstruction) of previous technologies – both biotechnologies and other forms of technology – in order to suggest an ethically robust approach to governance of biotechnologies that are currently being researched, such as synthetic biology, and others that may follow in the future. Our focus will be on how control is exercised over the shaping of research, development and innovation in biotechnologies, and the assumptions and values implied in this. If we are committed to a future in which biotechnologies play a significant part, how this control is exercised matters greatly. It cannot, however, be exercised through crude choices between different ready-made technologies; rather, it concerns the multiple determinations, by numerous actors in multiple contexts, of the conditions that direct, encourage, facilitate, restrict, limit and control biotechnology research, development and innovation. The conditions to which these choices relate include institutional design, funding and investment, law and regulation, and economic and commercial conditions, among many other things. More importantly, it is about the way in which these multiple determinations come together to affect the public interest.

[50] For example, this complaint has been levelled against the US National Institutes of Health-Department of Energy Joint Working Group on Ethical, Legal, and Social Issues (established as part of the Human Genome Project in 1989). For the most part, the Group was restricted in its remit to considering the implications of the project and the related science and technology, rather than whether the investment in the project should have been made in the first place. See: Human Genome News (1990) *NIH-DOE joint working group on ethical, legal, and social issues established*, available at: http://www.ornl.gov/sci/techresources/Human_Genome/publicat/hgn/v2n1/05elsi.shtml.

Chapter 2

Biotechnology promises and expectations

Chapter 2 - Biotechnology promises and expectations

Chapter overview

This Chapter begins with a recognition of the diversity of biotechnologies and the different ways in which people use the term. We offer an inclusive description of the field of technologies in which we are interested. We then briefly survey the main fields of biotechnology in which significant advances are currently taking place. These are:

- cellular biotechnologies, including regenerative medicine;
- molecular biotechnologies, including transgenic plants and animals, and pharmaceutical biotechnology;
- genomic medicine, including personalised medicine, gene therapy and bioinformatics;
- synthetic biology; and
- nanotechnologies and nanomedicine.

We observe that the picture in each of these fields is of uneven progress with impressive technical advances often halted by scientific obstacles and contingent factors such as commercial investment and legal changes. We note the difference between this picture and the typical prospectus offered for new biotechnologies. We note an optimism bias with regard to prospective biotechnologies and that timescales for innovation are typically overestimated.

We identify a reason for the optimism bias in the patterning of expectations by reflection on the experience of past technologies. We examine the role of collective visions of technology futures, popular narratives about progress and the presentation of biotechnology in popular culture in fostering and reinforcing over-exaggerated expectations (of benefits or harms).

We note, however, that the experience of past technologies is often not an appropriate basis for inferences about the prospects of technologies of the future: the experiences are often poorly selected (more prospective technologies fail than succeed) and of questionable relevance to qualitatively different technologies with distinctive constraints.

These reflections recommend a methodological scepticism when assessing claims about prospective biotechnologies in order to make the foundation of decision making more robust. This scepticism can open up a space for reflection that averts two significant dangers of the dominant discourses on emerging biotechnologies, those of:

- linking biotechnologies to particular social objectives and thereby ignoring other benefits and reasons to promote the development of biotechnologies, and
- linking social objectives to particular biotechnologies and thereby failing adequately to consider and explore alternative means of meeting those objectives.

Introduction

2.1 In Chapter 1, we discussed the impact of biotechnologies of the relatively recent past and outlined some of the issues with which we will be concerned in this Report: the way in which technologies come to be researched, developed, implemented and diffused, and the part that deliberate choice, chance and necessity can play in these processes. We now turn our attention to fields of research from which biotechnologies of the future are currently emerging or may emerge. In this Chapter we will describe how some of those fields have developed and the promises and expectations that have been associated with them. We also consider how these expectations may be formed, modified and influenced by events and ideas. Our purpose will be twofold: firstly to provide some concrete examples of the kind of biotechnologies that we are concerned with in this Report, and secondly to advance our argument by drawing attention to the relationship between research and innovation in biotechnology on one hand and, on the other, the way in which biotechnologies are represented and discussed in different contexts. This will clarify how different *discourses on biotechnologies* influence biotechnology governance, and therefore on the emergence of biotechnologies themselves.

In what developments are we interested?

2.2 While the definition of ‘technology’ is commonly understood, the usage of substantive terms ‘a technology’ and ‘a biotechnology’ are subject to some variation and vagueness. Many of the distinctions that are made within the field of biotechnology serve pragmatic purposes (for

example, to assign research to a funding stream), rather than being intrinsic to the technologies themselves.[51] In responses to our public consultation[52] and in the broader literature on biotechnologies, the term 'biotechnology' is used to refer to:

- broad 'fields' of knowledge (synthetic biology is a 'biotechnology' in this sense);
- programmes of research defined by specific objectives (genetic modification (GM) of food crops is a 'biotechnology' in this sense);
- techniques or procedures, often associated with a distinct kind of apparatus or machinery (DNA sequencing is a 'biotechnology' in this sense);
- specific applications of techniques or procedures (in vitro fertilisation (IVF) is a 'biotechnology' in this sense); and
- products themselves (a nanoscale biosensor device is a 'biotechnology' in this sense).

2.3 We have characterised biotechnologies as conjunctions of knowledge, practices, products and applications. We have adopted this characterisation to reflect our interest, in this Report, in how these elements are brought together. However, what distinguishes biotechnologies from other technological forms is that these conjunctions involve some biological element, system or process. We recognise that the term 'biological' can also be problematic and, indeed, that many of the most vivid controversies arise at the margins of its application (for example, at the interface between chemistry and biology). For pragmatic reasons, we use the term inclusively: it is not our intention to rule anything out of consideration, but rather to orientate ourselves in the direction of the biological without claiming to know precisely where it begins and ends. In view of our intention to examine cross-cutting issues raised by emerging biotechnologies generally, our interests include technologies that involve:

- the utilisation of an adapted or unadapted biological system, process or component in industrial production (for example, the use of animals as bioreactors or bacteria for biofuel production), and/or
- the modification of a biological system or process through addition, insertion or integration with a biological or non-biological component (for example, gene therapy, regenerative medicine, tissue engineering, transgenic crops), and/or
- the creation of a new biological product or system using biological or non-biological components (for example, bacteria- or plant-produced plastics, 'BioSteel'®, in vitro produced meat).

2.4 The difficulty of defining the class of biotechnologies as a whole and of drawing clear distinctions between different biotechnologies is compounded by the interweaving genealogy of emerging biotechnologies. The communication, convergence, cross-fertilisation and differentiation of knowledge is, undoubtedly, one reason for the apparent fecundity of the field. Nor are biotechnologies, however defined, uniformly either emerging or established: in each field there is a body of relatively accepted knowledge and practice, having reasonably well-established applications, and a constantly moving leading edge (often implying reinterpretation of established knowledge and reconfiguring of existing practice). Thus the label 'biotechnology'

[51] The distinction between genetic engineering and synthetic biology may not be absolute. For example, the production of a precursor for an anti-malarial drug (artemisinic acid), often cited as an instance of synthetic biology, may also be regarded as genetic engineering involving many genes. See: Ro DK, Paradise EM, Ouellet M *et al.* (2006) Production of the antimalarial drug precursor artemisinic acid in engineered yeast *Nature* **440**: 940-3, for details on the production of synthetic artemisinic acid.

[52] The Working Party's public consultation ran from April to June 2011. A summary of the responses, which contains a list of biotechnologies that respondents referred to in their submissions, can be found online at: http://www.nuffieldbioethics.org/emerging-biotechnologies/emerging-biotechnologies-consultation.

encompasses a number of established innovations connecting knowledge, practices, products and applications, but also other conjunctions in the process of being assembled.

Cellular biotechnologies

Regenerative medicine

2.5 The identification and isolation of stem cells in the 1960s opened up a new field of research into regenerative medicine, raising the possibility of replacing damaged or defective tissues.[53] Stem cells are the precursor cells of the different tissues that comprise the body. The properties of stem cells – their capacity for indefinite self-renewal and the ability to differentiate into more specialised cell types – give them a great range of potential applications. Stem cell research was given a significant boost by convergence with the science and techniques of embryology: in particular, the possibility of establishing laboratory stem cell lines from embryos[54] that have a capacity for differentiation into a large number of other cell types (pluripotency) has led to highly promising lines of research. Arguably, this promise has been central, in the UK, to securing a favourable disposition of the law and public attitudes to extending human embryo research for therapeutic purposes.[55] The applications at which stem cell research is aimed include treatment of a range of diseases (such as sickle-cell disease, anaemias and thalassaemias) and injuries (reconnecting damaged nerves after spinal injury to restore sensation and motor control). Other applications include disease modelling[56] and the production of *in vitro* models for pharmaceutical testing, to assess toxicity more effectively than in animal models and in a way that minimises the need for human trials.[57]

2.6 The 'holy grail' of stem cell research has, for many years, been the production of bespoke tissues for transplant. The initial hope was that 'therapeutic cloning' techniques could produce cell lines with the same genetic immunological characteristics as the person to be treated. Being able to produce such tissues would overcome both the lack of availability of suitable transplant tissue from human donors and the need to use immunosuppressant drugs in order to avoid the transplanted tissue being rejected by the recipient. If this could be achieved effectively, it would mean a potentially unlimited capacity to generate replacement tissues and even solid organs to replace diseased or damaged ones. However, stem cell research has encountered setbacks with therapeutic efficacy, tumour formation[58] and cell expansion, as well as ethical controversy heightened by the instrumental use of human embryos in some approaches. Progress with the translation of stem cell research into therapeutic applications has also been set back by commercial difficulties among leading innovators.[59] These difficulties are likely to be compounded by a ruling of the European Court of Justice[60] that excludes human embryo-derived inventions from patentability on ethical grounds, which may have significant repercussions for commercial investment in future human embryonic stem cell research.[61]

---

[53] See early works on identifying and isolating stem cells: Siminovitch L, McCulloch EA and Till JE (1963) The distribution of colony-forming cells among spleen colonies *Journal of Cellular and Comparative Physiology* **62**: 327-36; Altman J and Das GD (1967) Postnatal neurogenesis in the guinea-pig *Nature* **214**: 1098-101.

[54] Evans MJ and Kaufman MH (1981) Establishment in culture of pluripotential cells from mouse embryos *Nature* **292**: 154-6.

[55] For example, in the passage of the Human Fertilisation and Embryology (Research Purposes) Regulations 2001 (SI 2001 No.188) and Human Fertilisation and Embryology Act 2008.

[56] Grskovic M, Javaherian A, Strulovici B and Daley GQ (2011) Induced pluripotent stem cells — opportunities for disease modelling and drug discovery *Nature Reviews Drug Discovery* **10**: 915-29.

[57] For example, Stem Cells for Safer Medicines is a UK public-private collaboration developing stem cell resources for use in the early, high throughput, toxicology screening of potential new medicines. See: http://www.sc4sm.org.

[58] Gutierrez-Aranda I, Ramos-Mejia V, Bueno C *et al.* (2010) Human induced pluripotent stem cells develop teratoma more efficiently and faster than human embryonic stem cells regardless the site of injection *Stem Cells* **28**: 1568-70.

[59] For example, the withdrawal of the leading human embryonic stem cell firm, Geron, from therapeutic trials, citing scarcity of funding; see: Pollack A (2011) Geron is shutting down its stem cell clinical trial *The New York Times* 14 November, available at: http://www.nytimes.com/2011/11/15/business/geron-is-shutting-down-its-stem-cell-clinical-trial.html?_r=0. We will return to the issue of commercialisation of biotechnologies in Chapter 9.

[60] *Brüstle v. Greenpeace eV* (Case C-34/10), 18 October 2011.

[61] We discuss the importance of patenting for emerging biotechnologies in Chapter 9.

Molecular biotechnologies

2.7 One of the most significant advances in the field of biotechnology was the development of recombinant DNA technology in the early 1970s.[62] For the first time, this allowed the deliberate transfer of functionally characterised genes from one organism to another, with the aim of reproducing in the second organism the desirable traits identified in the first.

Genetic modification and selection of crops traits

2.8 One of the first biotechnology fields to catch the public imagination and galvanise opinions was agricultural biotechnology.[63] Despite the commercial failure of the first attempts to market GM tomatoes in the early 1990s,[64] take up of the technology in the US has since proceeded rapidly.[65] In the UK, by contrast, brief initial success with a similar product (Zeneca's GM tomato paste) was halted abruptly by poor sales.[66] Indeed, concern about the impact of GM crops on human health, the environment and economic wellbeing, has played a significant part in defining the political terrain of biotechnology policy in the UK and continental Europe,[67] with levels of distrust and suspicion aggravated by apparently poorly framed attempts on the part of policy makers to engage with them.[68]

2.9 These controversies have been further compounded, particularly with initiatives to introduce GM crops in developing economies, by concerns about economic and social implications, such as concentration of industrial supply chains, ownership of intellectual property, and selection of products and technologies that prioritise private producer benefits at the expense of public benefits. Although the main firms involved use alternatives such as marker-assisted and genomics-assisted breeding alongside GM (as these different strategies are likely to have different levels of effectiveness depending on the traits of interest), the major bottleneck with all of these technologies remains in identifying the combinations of genes and other conditions responsible for the traits of interest.

Transgenic animals

2.10 The power of recombinant DNA technology is that it has potential uses across all biological systems containing DNA. The same recombinant DNA techniques that allowed modification of plant traits can equally be used to breed animals with altered traits. Transgenic animals (with genes from different species inserted) are used routinely in research to identify gene function. For example, a gene (GFP) that gives rise to a fluorescent protein in jellyfish can be linked to gene sites in mammals to identify the protein encoded by the gene of interest by fluorescence. Transgenic animals have also been developed for industrial purposes through a procedure

---

62 The initial application to the US Patent Office describing the recombinant DNA technique was applied for by Stanford University and the University of California in 1974. See: Beardsley T (1984) Biotechnology: Cohen-Boyer patent finally confirmed *Nature* **311**: 3.

63 GM crops were the subject of two earlier Nuffield Council on Bioethics reports: Nuffield Council on Bioethics (1999) *Genetically modified crops: the ethical and social issues*, available at: http://www.nuffieldbioethics.org/gm-crops and Nuffield Council on Bioethics (2003) *The use of GM crops in developing countries: a follow-up discussion paper*, available at: http://www.nuffieldbioethics.org/gm-crops-developing-countries.

64 Calgene's 'FlavrSavr' tomato was modified to alter the ripening process. Zeneca, under licence, introduced a tomato paste based on the same modification into the UK market. Ultimately, both products failed commercially. See: Bruening G and Lyons JM (2000) *The case of the FLAVR SAVR tomato*, available at: http://ucanr.org/repository/CAO/landingpage.cfm?article=ca.v054n04p6&fulltext=yes. See also: House of Commons Science and Technology Committee (1999) *Scientific advisory system: genetically modified foods*, available at: http://www.publications.parliament.uk/pa/cm199899/cmselect/cmsctech/286/28602.htm, at paragraphs 11, 22 and 25.

65 Vàzquez-Salat N, Salter B, Smets G and Houdebine L-M (2012) The current state of GMO governance: are we ready for GM animals? *Biotechnology Advances* **30**: 1336–43.

66 House of Commons Science and Technology Committee (1999) *Scientific advisory system: genetically modified foods*, available at: http://www.publications.parliament.uk/pa/cm199899/cmselect/cmsctech/286/28602.htm, paragraph 21ff.

67 See: Gaskell G, Einsiedel E, Priest S *et al.* (2001) Troubled waters: the Atlantic divide on biotechnology policy, in *Biotechnology 1996-2000: the years of controversy*, Gaskell G, and Bauer MW (Editors) (London: Science Museum).

68 Horlick-Jones T, Walls J, Rowe, G, Pidgeon N, Poortinga W and O'Riordan T (2004) *A deliberative future? An independent evaluation of the GM Nation? Public debate about the possible commercialisation of transgenic crops in Britain, 2003.* (Norwich: University of East Anglia).

known as 'pharming'. This involves using modified animals as 'bioreactors' to produce substances beneficial to humans. These include insulin for the treatment of diabetes and vaccines, which may be extracted, for example, from the animals' milk. Another example is the development of a method of producing an anticoagulant drug (ATryn) that involves extracting it from the milk of a transgenic goat. This was approved for use by the US Food and Drug Administration (FDA) in February 2009, and was the FDA's first approval of a biological product produced by a transgenic animal.[69] Another example is 'BioSteel®', the proprietary name for a protein extracted from the milk of transgenic goats that had been modified with genes related to the production of spider silk.[70] This product was expected to have a huge number of potential applications from medical sutures to body armour, although there have been difficulties in 'scaling up' to commercial production levels and the firm (Nexia) that produced it turned its attention to other military applications before it ceased trading in 2006. Research in this area – for example using transgenic silkworms – nevertheless continues, with a new firm, Kraig Biocraft Laboratories, established to commercialise research at the universities of Wyoming and Notre Dame in the US.[71]

Xenotransplantation

2.11 Transgenic animals have also been developed for the purposes of xenotransplantation (cross-species transplantation), in particular GM pigs.[72] Non-human, decellularised structural tissues such as pig heart valves have been used in surgical procedures for several decades and there has also been considerable research into the xenotransplantation of whole organs, tissues and cells. Xenotransplantation research has been performed since the mid-20th Century, but suffered considerable setbacks during the 1970s and 1980s (such as short survival periods of organ recipients following baboon-to-human transplants and what was considered then as the "insurmountable" problem of rejection).[73] However, recent advances in some areas, in particular the wide availability of pigs genetically modified for the purposes of transplantation, have led to considerable progress in xenotransplantation research during the last decade.[74] Although routine clinical xenotransplantation has yet to become a reality,[75] some authors note that – at least for tissues and cells, if not organs – there is a possibility that clinical implementation may occur in the near future.[76]

Pharmaceutical biotechnology

2.12 The current strategic focus of publicly funded life sciences research in the UK is largely on medical applications of biotechnology.[77] Biological drugs – recombinant proteins, such as insulin,[78] and monoclonal antibodies, such as trastuzumab ('Herceptin'®), which may be used to treat breast cancer – have been developed and introduced with varying degrees of success.

---

69 See: US Food and Drug Administration (2009) *FDA approves orphan drug ATryn to treat rare clotting disorder*, available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm109074.htm.

70 Lazaris A, Arcidiacono S, Huang Y *et al.* (2002) Spider silk fibers spun from soluble recombinant silk produced in mammalian cells *Science* **295**: 472-6.

71 See: University of Notre Dame (29 September) *Notre Dame and University of Wyoming scientists genetically engineer silkworms to produce artificial spider silk*, available at: http://newsinfo.nd.edu/news/16934-notre-dame-and-university-of-wyoming-scientists-genetically-engineer-silkworms-to-produce-artificial-spider-silk.

72 Klymiuk N, Aigner B, Brem G and Wolf E (2009) Genetic modification of pigs as organ donors for xenotransplantation *Molecular Reproduction and Development* **77**: 209-21.

73 Persidis A (1999) Xenotransplantation *Nature Biotechnology* **17**: 205-6.

74 Such pigs have been modified in a number of ways, such as to prevent porcine endogenous retroviruses activation or to reduce or eliminate the expression of particular pig antigens, which can help to limit incidences of hyperacute rejection when transplanting into primates. See: Ekser B, Ezzelarab M, Hara H *et al.* (2011) Clinical xenotransplantation: the next medical revolution? *The Lancet* **379**: 672-83.

75 Dalmasso AP (2012) On the intersections of basic and applied research in xenotransplantation *Xenotransplantation* **19**: 137-43.

76 Ibid.

77 Department for Business, Innovation and Skills (2011) *Strategy for UK life sciences*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences.

78 The first genetic engineering firm, Genentech, was founded in 1976 to "develop a new generation of therapeutics created from genetically engineered copies of naturally occurring molecules important in human health and disease"; the firm began producing recombinant insulin from modified *E.coli* bacteria in 1978. See, generally, the Genentech website, especially the 'History' section, at: http://www.gene.com/gene/about/corporate/history/index.html.

Biotechnology has also had an impact on drug discovery and drug development,[79] offering a 'rational design' approach to developing drugs for targets identified through genetic sequencing as an alternative to traditional drug discovery protocols that screen candidate substances for likely therapeutic efficacy. Nevertheless, use of biotechnology approaches to benefit patients, as opposed to producers, has been questioned by some[80] while, in any case, the rate of appearance of new biopharmaceuticals has proved significantly lower than had been hoped.[81]

2.13 Another field of research within biomedical science has focused on preventing the progression of disease by silencing the genes responsible for the replication of cancers and infectious agents. 'Antisense' research from the late 1970s involved introducing a strand of ribonucleic acid (RNA) with a molecular composition that would bind to genes identified as responsible for replication of disease and suppress their expression.[82] However, the research encountered significant obstacles to therapeutic use, including difficulty in delivering antisense RNA to target locations and avoiding digestion by the body's natural defensive mechanisms. From 1998, when it was first demonstrated in animals,[83] attention shifted to RNA interference (RNAi) involving double stranded short interfering RNAs (siRNAs), which occur naturally and are thought to be significantly more effective than single stranded antisense.[84] Pharmaceutical firms are working on RNAi-based therapies in areas including pain killers, slimming aids, and cancer[85] and scientists have discovered many new classes of RNAs that are thought to be involved in a range of common diseases, including leukaemia, lung cancer, hepatitis C, and diabetes.[86] Scientists have suggested that the RNA interference effect is just the tip of the iceberg of a complex interconnecting network of gene regulation, which is still incompletely understood.[87] However, despite an early rush for patents in this area, the promise of this technology for therapeutic use has not yet been realised. As the problem of delivering the siRNAs to target sites in the body has proved durably resistant to solution,[88] many firms have begun to withdraw investment from this area.[89]

Genomic medicine

2.14 Personalised medicine is a concept that reflects a confluence of different scientific, technological and social disciplines and approaches. A previous Nuffield Council on Bioethics report on personalised health care considered in depth the notion of 'personalisation' in the context of medicine and health care.[90] It noted how personalisation may have a number of different meanings, but among these is the tailoring of medicine to the biological characteristics

[79] See: Galambos L and Sturchio JL (1998) Pharmaceutical firms and the transition to biotechnology: a study in strategic innovation *Business History Review* **72**: 250-78.

[80] Hopkins, Nightingale, Kraft and Mahdi noted "biopharmaceuticals, like NCEs before them, are increasingly focused on securing economic benefits for developers rather than clinical benefits for patients in areas of unmet medical need." Hopkins MM, Martin PA, Nightingale P, Kraft A and Mahdi S (2007) The myth of the biotech revolution: an assessment of technological, clinical and organisational change *Research Policy* **36**: 566-89. This may, of course, be due to the commercial conditions of innovation, which we discuss in Chapter 9, rather than inherent limitations of the technology.

[81] Ibid.

[82] Zamecnik PC and Stephenson ML (1978) Inhibition of Rous sarcoma virus replication and cell transformation by a specific oligodeoxynucleotide *Proceedings of the National Academy of Sciences* **75**: 280-4.

[83] Fire A, Xu SQ, Montgomery MK *et al.* (1998) Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans *Nature* **391**: 806-11.

[84] Elbashir SM, Harborth J, Lendeckel W *et al.* (2001) Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells *Nature* **411**: 494-8.

[85] Economist editorial (2007) Really new advances *The Economist* 14 June, available at: http://www.economist.com/node/9333471.

[86] Mack GS (2007) MicroRNA gets down to business *Nature Biotechnology* **25**: 631-8.

[87] Amaral PP, Dinger ME, Mercer TR and Mattick JS (2008) The eukaryotic genome as an RNA machine *Science* **319**: 1787-9.

[88] Leng Q, Woodle MC, Lu PY and Mixson AJ (2009) Advances in systemic siRNA delivery *Drugs of the Future* **34**: 721.

[89] Ledford H (2010) Drug giants turn their backs on RNA interference *Nature* **468**: 487.

[90] Nuffield Council on Bioethics (2010) *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, available at: http://www.nuffieldbioethics.org/personalised-healthcare-0.

of particular patients or patient groups (pharmacogenetics, stratified medicine).[91] The basic enabling technology for personalised medicine is molecular diagnostics.

Personalised medicine

2.15 Much of the interest in this area relates to genomic medicine developed alongside and as a result of the Human Genome Project (HGP) and associated research (such as the HapMap,[92] ENCODE[93] and various genome-wide association studies). During the early years of the 21st Century there was considerable discussion of how the completion of the HGP would lead to a new era of medicine – one focused on prediction and prevention rather than cure.[94] This would grow out of more powerful diagnostic techniques (such as monogenic or multifactorial genetic tests) and the use of this information to inform lifestyle changes, tailored pharmaceuticals or gene therapy. Despite the enthusiasm surrounding the completion of the HGP, however, and in common with other biotechnologies, the innovation system for genomics in health care has proved a more complex matter than simple technical diffusion.[95]

Gene therapy

2.16 Another emerging area of biomedicine is gene therapy, which involves treating disease caused by faulty genes or gene function by the introduction of new therapeutic genes directly into the patient's cells by means of delivery mechanisms (vectors), such as modified viruses. Although not dependant on the performance of the HGP (there were gene therapy trials in 1990, the year the HGP began), the identification of genetic mutations responsible for disease made possible by the HGP has greatly facilitated scientific research in gene therapy.[96] This field, too, has suffered from setbacks in clinical trials and the impact of these on commercial interest in gene therapy research.[97] More recent trial results, for a range of conditions including Parkinson's disease,[98] have led to renewed optimism among researchers in the field.

Bioinformatics and converging technologies

2.17 Information and Communications Technology (ICT) has had, and will continue to have, a significant role in the development of personalised medicine:[99] the (relatively) recent – and rapid – improvement in the global capacity to store, transmit and compute large quantities of data has had a profound impact on all the sciences, including biology and especially genetics.[100] Some have argued that the demands of medicine-related ICT will soon surpass those of other data intensive fields and that the realisation of a genuinely personalised medicine will rely upon sophisticated computer models of living people.[101] For example, the 'IT Future of Medicine'

---

[91] Pharmacogenetics was also the subject of a separate Council report. See: Nuffield Council on Bioethics (2003) *Pharmacogenetics: ethical issues*, available at: http://www.nuffieldbioethics.org/pharmacogenetics.

[92] The HapMap is "a haplotype map of the human genome…which will describe the common patterns of human DNA sequence variation". See: International Haplomap Project (2006) *About the International HapMap Project*, available at: http://hapmap.ncbi.nlm.nih.gov/abouthapmap.html.

[93] 'ENCODE' refers to the Encyclopedia of DNA Elements, a project which aims to identify all functional elements in the human genome sequence and develop technologies to generate high throughput data on those elements. See: National Human Genome Research Institute (2012) *ENCODE Overview*, available at: https://www.genome.gov/10005107.

[94] See, for example, Subramanian G, Adams MD, Venter JC and Broder S (2001) Implications of the human genome for understanding human biology and medicine *JAMA* **286**: 2296-307.

[95] As a recent report from the PHG Foundation observes: "the prevailing rhetoric amongst basic science funders, researchers and many policy-makers both in UK and worldwide is that genomic medicine represents a revolution in healthcare"; however: "knowledge and experience is slowly gained by clinical research leaders and the process of embedding new practice in high quality care pathways throughout the UK is gradual and difficult." See: Burton H, Cole T and Farndon P (2012) *Genomics in medicine: delivering genomics through clinical practice*, available at: http://www.phgfoundation.org/reports/12093, p16.

[96] Goncz KK, Prokopishyn NL, Chow BL, Davis BR and Gruenert DC (2002) Application of SFHR to gene therapy of monogenic disorders *Gene Therapy* **9**: 691-4.

[97] Nature editorial (2009) Gene therapy deserves a fresh chance *Nature* **461**: 1173.

[98] LeWitt PA, Rezai AR, Leehey MA *et al.* (2011) AAV2-*GAD* gene therapy for advanced Parkinson's disease: a double-blind, sham-surgery controlled, randomised trial *The Lancet Neurology* **10**: 309-19.

[99] See, generally, Nuffield Council on Bioethics (2010) *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, available at: http://www.nuffieldbioethics.org/personalised-healthcare-0.

[100] Indeed, the HGP would not have been possible without such advances.

[101] See: Wiederhold BK (2012) ICT: this transformer isn't science fiction *Cyberpsychology, Behavior, and Social Networking* **15**: 189.

project (ITFoM) has the ambition to "create the entirely new ICT that is necessary to enable models of human biochemical pathways, cells, tissues, diseases and ultimately of the human as a whole" in order to "identify personalised prevention/therapy schedules and side effects of drugs".[102]

Synthetic biology

2.18 Synthetic biology applies the knowledge and tools developed in analytical biology to synthesise biological entities. It might be understood as an extension of genetic engineering, drawing on expertise in molecular biology, computer science, chemistry, and engineering. While some argue that the difference between synthetic biology and genetic engineering is largely one of labelling, others treat them as distinct fields of research.[103] An early inspiration, at least for some biologists using a synthetic approach, was a desire to understand natural biological systems,[104] although engineers working in synthetic biology focus primarily on producing novel applications. The definition of the field is subject to ongoing debate.[105] Its aims are usually taken to include exercising control at the level of design, characterisation and construction, to increase the predictability of designed biological systems.

Engineering biology

2.19 A range of different research activities fall under the broad heading of synthetic biology. Parts-based approaches aim to construct standardised biological parts (normally made of DNA). The ambition is to design them so that they are interchangeable and can be combined in a modular fashion to make new biological devices, making biology easier to engineer.[106] The most well-known type of biological part is a 'BioBrick'®, a standardised, interchangeable, composable DNA sequence of defined structure and function, developed with a view to building biological systems in living cells.[107]

2.20 Alternative approaches include attempts to simplify existing genomes to make a 'chassis' which, it is hoped, will form a basis for new synthetic organisms that will perform useful functions (such as producing biofuels).[108] In 2010, one research group reported the creation of an entirely synthetic version of the natural genome of a bacterium (*Mycoplasma mycoides*) that was put into a recipient cell, which then replicated successfully.[109] Other approaches attempt to reconstruct existing viral genomes from scratch, including the polio virus[110] and the φX174

[102] Lehrach H, Subrak R, Boyle P *et al.* (2011) ITFoM – the IT future of medicine *Procedia Computer Science* **7**: 26-9.

[103] For example, the European Commission, the UK Royal Society, the UK Royal Academy of Engineering and the UK Biotechnology and Biological Sciences Research Council (BBSRC) have all produced material treating synthetic biology as a separate field. See, respectively: European Commission (2005) *Synthetic biology: applying engineering to biology*, available at: ftp://ftp.cordis.europa.eu/pub/nest/docs/syntheticbiology_b5_eur21796_en.pdf; Zhang YW, Marris C and Rose N (2011) *Transnational governance of synthetic biology: Scientific uncertainty, cross-borderness and the 'art' of governance*, available at: http://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/publications/2011/4294977685.pdf; The Royal Academy of Engineering (2009) *Synthetic biology: scope, applications, and implications* available at: http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf; and, Balmer A and Martin P (2008) *Synthetic biology: social and ethical challenges - an independent review commissioned by the Biotechnology and Biological Sciences Research Council*, available at: http://www.bbsrc.ac.uk/web/FILES/Reviews/0806_synthetic_biology.pdf.

[104] Elowitz MB and Leibler S (2000) A synthetic oscillatory network of transcriptional regulators *Nature* **403**: 335-8.

[105] See, for example, O'Malley MA, Powell A, Davies JF and Calvert J (2007) Knowledge-making distinctions in synthetic biology *BioEssays* **30**: 57-65.

[106] Brent R (2004) A partnership between biology and engineering *Nature Biotechnology* **22**: 1211-4.

[107] The BioBrick Public Agreement, an attempt to make biological parts free for others to use, was launched at SB5.0 in June 2011. See: BioBricks Foundation (2012) *The BioBrick™ Public Agreement (BPA)*, available at: http://biobricks.org/bpa.

[108] Glass JI, Assad-Garcia N, Alperovich N *et al.* (2006) Essential genes of a minimal bacterium *Proceedings of the National Academy of Sciences* **103**: 425-30. In May 2007 the J. Craig Venter Institute filed a patent for the smallest genome needed for a living organism. See also the relevant patent application for this approach: Glass JI, Smith HO, Hutchinson CA, Alperovich N Assad-Garcia N (2007) *Minimal bacterial genome* United States Patent Application No 11/546,364 (filed Oct 12, 2006).

[109] Gibson DG, Glass JI, Lartigue C *et al.* (2010) Creation of a bacterial cell controlled by a chemically synthesized genome *Science* **329**: 52-6. Commentators are divided over how revolutionary this step has been: Bedau M, Church G, Rasmussen S *et al.* (2010) Life after the synthetic cell *Nature* **465**: 422-24. See also footnote 215.

[110] Cello J, Paul AV and Wimmer E (2002) Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template *Science* **297**: 1016-8.

bacteriophage.[111] The purpose of this research is to generate knowledge that could, for example, lead to new synthetic vaccines in response to viruses that are themselves "diverse and variable", such as those that cause severe acute respiratory syndrome and hepatitis C.[112] On a wider scale, protocell research involves the attempt to recreate living cells from very simple components,[113] with the aim of creating new forms of life.[114]

Metabolic pathway engineering

2.21 A related area that has been researched since the since the 1990s is the manipulation of existing metabolic pathways to produce new products, the most well-known example of which is the construction of an artificial metabolic pathway in *E. coli* and yeast to produce a precursor (arteminisinic acid) for an anti-malarial drug.[115] It has been suggested that an approach such as this could be used to produce therapeutically useful compounds for the treatment of cancer and HIV[116], as well as polyketides,[117] a class of drugs with a variety of uses, such as the production of antibiotics[118] and insecticides.[119] This approach is also being used to produce biofuels, although firms are currently experiencing difficulties in scaling-up production to commercially viable levels.[120]

Alternative biologies

2.22 Whereas these approaches involve pushing the boundaries of natural systems in order to learn more about them, 'xenobiology' research attempts to make a biology that is altogether different from that which is found in nature.[121] An example of this approach is the attempt to use different kinds of nucleic acid – for example 'xeno-nucleic acid' – as opposed to the familiar RNA or DNA that occur in nature.[122]

2.23 In its current incarnation, synthetic biology is a young field[123] which means that most of the discussion around it is prospective and promissory, with only a few examples, such as the production of artemisinic acid, drawn on repeatedly to justify its promise. In practice, synthetic biologists continually confront the complex and context-dependent nature of biological systems.[124] However, in recent years the field has generated much enthusiasm and, increasingly, funding, because it is application-oriented and is seen by governments as a potential source of economic growth.[125]

---

[111] Smith HO, Hutchison III CA, Pfannkoch C and Venter JC (2003) Generating a synthetic genome by whole genome assembly: φX174 bacteriophage from synthetic oligonucleotides *Proceedings of the National Academy of Sciences* **100**: 15440-5.
[112] Garfinkel MS, Endy D, Epstein GL and Friedman RM (2007) *Synthetic genomics: options for governance*, available at: http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-genomics-report/synthetic-genomics-report.pdf.
[113] Deamer D (2005) A giant step towards artificial life? *Trends in Biotechnology* **23**: 336-8.
[114] Bedau MA and Parke EC (Editors) (2009) *The ethics of protocells: moral and social implications of creating life in the laboratory* (Cambridge, Massachusetts: MIT Press).
[115] Ro DK, Paradise EM, Ouellet M *et al.* (2006) Production of the antimalarial drug precursor artemisinic acid in engineered yeast *Nature* **440**: 940-3.
[116] Voigt CA and Keasling JD (2005) Programming cellular function *Nature Chemical Biology* **1**: 304-7.
[117] Heinemann M and Panke S (2006) Synthetic biology — putting engineering into biology *Bioinformatics* **22**: 2790-9.
[118] See: Baltz RH (2006) Molecular engineering approaches to peptide, polyketide and other antibiotics *Nature Biotechnology* **24**: 1533-40.
[119] Martin CJ, Timoney MC, Sheridan RM *et al.* (2003) Heterologous expression in Saccharopolyspora erythraea of a pentaketide synthase derived from the spinosyn polyketide synthase *Organic & Biomolecular Chemistry* **1**: 4144-7.
[120] Bullis K (2011) Why Amyris is focusing on moisturizers, not fuel, for now *Technology Review* 9 May, available at: http://www.technologyreview.com/news/427890/why-amyris-is-focusing-on-moisturizers-not-fuel.
[121] Schmidt M (2010) Xenobiology: a new form of life as the ultimate biosafety tool *BioEssays* **32**: 322-31.
[122] Pinheiro VB, Taylor AI, Cozens C *et al.* (2012) Synthetic genetic polymers capable of heredity and evolution *Science* **336**: 341-4.
[123] The term can be traced back to 1912 to Leduc's book *La biologie synthétique,* but the first conference called 'Synthetic Biology' (Synthetic Biology 1.0) was not held until 2004 at MIT. See: Syntheticbiology.org (2004) *The first international meeting on synthetic biology*, available at: http://syntheticbiology.org/Synthetic_Biology_1.0.html.
[124] Kwok R (2010) Five hard truths for synthetic biology *Nature* **463**: 288-90.
[125] See, for example, the 4 January 2012 speech 'Our hi-tech future' by the Minister for Universities and Science: http://www.bis.gov.uk/news/speeches/david-willetts-policy-exchange-britain-best-place-science-2012.

Nanotechnology

2.24 Nanotechnology, like synthetic biology, is not a single technology; instead it refers to a wide range of techniques and methods for manipulating matter on length scales from a nanometre – i.e. the typical size of molecules – to hundreds of nanometres, with the aim of creating new materials and devices. Some of these methods represent the incremental evolution of well-established techniques of applied physics, chemistry and materials science. In other cases, the techniques are at a much earlier stage, with promises about their future power being based on simple proof-of-principle demonstrations.

Nanoscale techniques

2.25 The most immediate impact of nanotechnology on the life sciences has been the use of new tools for investigating the nanoscale. Techniques such as optical tweezers have, since their introduction in the 1980s, allowed the properties of individual biomolecules and assemblies of biomolecules to be studied in conditions close to those found in nature. This has permitted the quantitative analysis of the mode of operation of biological machines such as molecular motors and ribosomes, as part of the new field of single molecule biophysics.[126] Other nanoscale technologies – such as quantum dots – have offered useful, though not transformative, additions to the experimental arsenal of cell biologists.[127] One long-standing ambition of bionanotechnology, which is potentially transformative, is the ability to read the sequence of bases of a single DNA molecule, dramatically reducing the time and cost of whole genome sequencing.[128]

Nanodevices

2.26 Biological inspiration underlies the idea of using DNA synthesised to a prescribed sequence as a building material for quite complex nanoscale structures, exploiting the precise rules of base-pairing to design desired self-assembly characteristics.[129] In the last ten years a series of new concepts have been demonstrated, including that DNA can be used as the basis, not just of nanoscale structures, but also of functional devices such as motors and logic gates,[130] as well as for efficient storage of diverse forms of information.[131] This field is becoming increasingly attractive as a result of continuing exponential falls in the cost of DNA synthesis and the increasing sophistication of the devices being created in the growing number of laboratories working in this field. Hybrid constructions involving biological molecular machines integrated with artificial nanostructures have also yielded striking demonstrations (for example "nano-propellers" powered by the biological rotary motor F1-ATPase)[132] and suggested potentially beneficial applications such as artificial photosynthesis combining functioning biological sub-cellular systems in synthetic constructs.

Nanomedicine

2.27 In the area of nanomedicine, there are already applications of nanotechnology in clinical use,[133] although, as in all the fields we discuss, the choice of terminology is underdetermined, and is

[126] See, for example: University of Oxford Department of Physics (2009) *Oxford molecular motors*, available at: http://www.physics.ox.ac.uk/berry/research/Techniques/Tweezers.
[127] Barroso MM (2011) Quantum dots in cell biology *Journal of Histochemistry and Cytochemistry* **59**: 237-51.
[128] For recent developments in genetic sequencing, see Box 9.1.
[129] Seeman NC and Lukeman PS (2004) Nucleic acid nanostructures: bottom-up control of geometry on the nanoscale *Reports on Progress in Physics* **68**: 237.
[130] Seelig G, Soloveichik D, Zhang DY and Winfree E (2006) Enzyme-free nucleic acid logic circuits *Science* **314**: 1585-8.
[131] Church GM, Gao Y and Kosuri S (2012) Next-generation digital information storage in DNA *Science* **337**: 1628.
[132] Soong RK, Bachand GD, Neves HP *et al.* (2000) Powering an inorganic nanodevice with a biomolecular motor *Science* **290**: 1555-8.
[133] Nano-oncology is a particularly good example of this, with several nanomedical applications either current or emerging. See, for example, the 2005 FDA approval of the drug 'Abraxane'® (an albumin-bound form of paclitaxel) for "treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy." The drug has a mean particle size of approximately 130 nanometres. See: US Food and Drug Administration

thus open to manipulation and historical reappraisal. The distinction is blurred, for example, between some older products, which used quite sophisticated formulation science, and what are now described as nanomedicines.[134] The potential contribution of nanotechnology to biomedicine is most obvious in addressing the significant challenges of drug delivery that bedevilled – and in some cases, thwarted – the development of biopharmaceuticals. The hope is that these may liberate entirely new classes of therapeutic substances. A number of physical and chemical mechanisms have been proposed by which nanoscale delivery devices might preferentially deliver a drug to a target, such as a solid tumour, or carry it across an otherwise impenetrable obstacle, such as the blood-brain barrier.[135] This has potentially important applications in facilitating the use of new therapeutic agents, such as proteins and antibodies,[136] nucleic acids (in the context of gene therapy or siRNA)[137] and stem cells and tissue engineering.[138] However, some of the earliest and most straightforward achievements of nanomedicine are expected to be in reformulating existing drugs to improve their efficacy and reduce their side-effects (incidentally extending the profitable lifetime of a drug after the expiry of an original period of patent protection).[139]

Timescales of emergence: a cross-cutting theme

2.28 From this brief survey of some of the current landscape of emerging biotechnologies, at least one cross-cutting theme emerges: it is that innovation in emerging biotechnologies typically takes much longer and is subject to many more vicissitudes than had been anticipated. This is due, to a significant degree, to the complexity and dynamics of the material conditions that make up the innovation system: funders committing and withdrawing investment, changing regulatory requirements, even geopolitical developments affecting the relative desirability of different military applications. In many cases, development of the original 'target' applications is derailed and the technology develops along a different pathway, finding expression in alternative, often unanticipated, conjunctions. Thus: 'BioSteel'® development moves from goats to silkworms, while the firm originally committed to developing it took its goats into the development of an antidote for nerve gas;[140] stem cell research initially focused on therapeutic applications has yielded a more immediately promising offshoot in predicting toxicity of medicinal compounds;[141] the microorganisms developed for biofuel production have found more profitable employment in the production of higher value products, including cosmetics.[142] The

(2005) *Approval package for application number 21-660*, available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2005/21660_ABRAXANE_approv.PDF and, more generally, Portney NG and Ozkan M (2006) Nano-oncology: drug delivery, imaging, and sensing *Analytical and Bioanalytical Chemistry* **384**: 620-30.

134 See: Duncan R and Gaspar R (2011) Nanomedicine(s) under the microscope *Molecular Pharmaceutics* **8**: 2101-41.

135 Farokhzad OC and Langer R (2009) Impact of nanotechnology on drug delivery *ACS Nano* **3**: 16-20.

136 Proteins and protein fragments, such as antibodies, can intervene with great specificity with biological processes at the molecular level, but in their bare form they are rapidly eliminated. 'Cimzia'®, approved in 2008 by the FDA for Crohn's disease, and in 2009 by the European Medicines Agency (EMEA) for arthritis, is a fragment of an antibody coupled to a water-soluble polymer. See: FDA (2008) *FDA approves Cimzia to treat Crohn's disease*, available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116882.htm and EMEA (2012) *Cimzia*, available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001037/human_med_001294.jsp&mid=WC0b01ac058001d124.

137 These, similarly, are difficult to deliver to a specific target without them being detected and destroyed by the body. (For siRNA see above, paragraph 2.13).

138 It is becoming clear that the fate of stem cells as they differentiate is strongly influenced by the local nanoscale mechanical properties and biochemical environment. See: Discher DE, Mooney DJ and Zandstra PW (2009) Growth factors, matrices, and forces combine and control stem cells *Science* **324**: 1673-7.

139 For example, 'Abraxane'®, which was approved by the FDA in 2005 (see footnote 133) is a nanoparticle-based formulation of an older anticancer drug (paclitaxel) which avoids the need to use a toxic solvent. 'Caelyx'® and 'Doxil'® are alternative names for a nanoscale formulation of another old anticancer drug called doxorubicin which was used in the EU and US respectively. This form was approved by the FDA in 1995, and the drug is encapsulated in molecular containers made from self-assembled lipid molecules. See: FDA (2012) *Drugs @ FDA*, available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm.

140 See PR Newswire (2004) *Nexia's military biotech drug Protexia® shows promise as a rescue therapy for civilian CW casualties*, available at: http://www.prnewswire.com/news-releases/nexias-military-biotech-drug-protexiar-shows-promise-as-a-rescue-therapy-for-civilian-cw-casualties-75819222.html.

141 California Institute for Regenerative Medicine (2008) *Stem cells in predictive toxicology: CIRM workshop report, July 7-8*, available at: http://www.cirm.ca.gov/pub/pdf/CIRM_Predictive_Tox.pdf.

142 See footnote 120.

path of biotechnology innovation is seldom either short or straight. If the pathway is imagined prospectively, as it often is, as one leading from basic research and proof of concept to marketable application, it is certainly long enough for political, commercial, medical or military priorities to change several times.

Biotechnology visions

2.29 Biotechnology research has made significant – sometimes extraordinary – advances, although these have rarely been made in a linear fashion. The advance towards imagined applications has often been held up, diverted, sometimes thwarted, by a variety of factors including investment decisions (stem cells, gene therapy, RNAi), public attitudes (GM crops), and ethical and legal constraints (embryonic stem cells), as well as bottlenecks and unforeseen intractabilities of biological science (for example, antisense, gene therapy, xenotransplantation). These factors are clearly not independent of one another: for example, longer than anticipated timeframes, or public opposition, or the appearance of a promising alternative, may lead to withdrawal of investment (as we shall consider in Chapter 9). Nor can they often be anticipated (as we shall consider in Chapter 3), although scientific researchers are, by professional disposition, usually wary of making definite predictions or ambitious claims.

2.30 However, the professional caution and scepticism of researchers is only one influence operating in what we have described as the discursive context surrounding biotechnologies, in which the interests and values of politicians, publics, entrepreneurs, media and institutions all play a part. Even if researchers, therefore, are able to resist the often considerable pressures to overstate their cautious and sober assessments of the prospects of emerging biotechnologies, others may still place a different construction on them. It is therefore not the formation of these representations in any one discursive context that is *necessarily* the source of dissonance, but their translation from one discursive context, in which they may appear with appropriate caveats and qualifications, into another in which they take up a place in relation to a *different* set of values and priorities. In other words, what is reported in a scientific journal can look very different when it is reported in the popular media. As we argued in Chapter 1, these representations are not inconsequential, because they can come to dominate the discourse through which conditions (like funding, investment, public support) that shape the emergence of biotechnologies generally are set. In the remainder of this Chapter we therefore begin to look at the formation of expectations and the role these play in emerging biotechnology governance.

The formation of expectations

2.31 Emerging biotechnologies are promissory by nature. Belief in the beneficial prospects of a particular biotechnological initiative is necessary, but not sufficient, to bring that technology about; on the other hand, scepticism about those prospects may be sufficient, but not necessary, to cause it to fail.

2.32 The securing of beliefs about the likelihood of future states of affairs, however, is dependent not only (or not even) on rational calculation but also on how expectation is structured by language, values and experience, and indeed how those come together in influential 'folk narratives'. An example of this is the frequently repeated assertion that the effects of a technology (positive or negative) tend to be overestimated in the short term and underestimated in the long term.[143] Observations of this kind have become powerful in structuring expectations about future biotechnologies but also in informing decisions that can contribute to bringing them about. For example, the Gartner consultancy's 'hype cycle' methodology offers an example of a structuring of expectation explicitly intended to inform choices that, for example, industrial decision makers might make, which might thereby contribute to bringing about the intended outcome through

[143] This observation, usually attributed to US scientist, Roy Amara, was used approvingly in 2010 in relation to the development of personalised medicine as an outcome of the HGP by the Francis Collins, the director of the US National Institutes of Health who described it as "the first law of technology". Collins F (2010) Has the revolution arrived? *Nature* **464**: 674-5.

their financial investment.[144] The 'hype cycle' consists of a curve that describes the 'visibility' of a technology through time, with the intention of helping investors to decide when to invest according to their 'individual appetite for risk'. It begins with a 'peak of inflated expectations' that are generated by an apparent technological breakthrough leading to some early successes and accompanied by significant publicity. Then, as the technology later fails to live up to its early promise, its visibility declines into a 'trough of disillusionment', a critical period in which it may be kept afloat only by surviving early adopters, before new generation products can be generated, and understanding and applications gradually spread (the 'slope of enlightenment'), until a point is reached at which mainstream adoption begins to take hold (the 'plateau of productivity').

2.33 Giving priority to visions of particular biotechnology outcomes – of fully realised conjunctions of knowledge, practice, products and application, and of their place in the imagined future state of the world that they help to make possible – tends to have the two significant effects. Firstly, it 'foreshortens' perceptions of the timescale for the realisation of benefits.[145] Secondly, it 'tunnels' both technology policy and social policy to the detriment of both. It does this, on one hand, by narrowing the way that technology is appreciated to an assessment of its ability to deliver specific outcomes rather than its broader, albeit largely unforeseeable, potential; secondly, it narrows the consideration of the possible ways of achieving social ends to expectations placed on particular technologies. For example, if the 'vision' is to develop third generation biofuels to mitigate climate change, then there can be a tendency to see the benefits of these biofuels *only* in terms of their effect on climate change (and not in relation to other things such as their potential benefits to non-fossil fuel rich economies, even if they do not actually limit global warming). On the other hand, it is not *only* the development of third generation biofuels that can mitigate climate change, and the question of how available resources should be distributed between different approaches is an important one strategically, which may be significantly foreclosed once a dominant vision takes hold. As well as under-representing the complexity and contingency of the innovation process, such 'foreshortening' and 'tunnelling' of expectations may also limit the appreciation of the opportunities for governance and control.[146]

Imported technological visions

Future visions

2.34 One of the ways in which attitudes to prospective technologies are construed is in terms of the kind of world that technological developments may bring about. These commonly incorporate features such as longevity, health into old age, free electricity or power, and inexpensive consumption, with corresponding dystopias, such as decimation by mutant pandemic viruses or the emergence of a 'genetic underclass'. This kind of anticipation may be called the 'sociotechnical imaginary' or 'technoscientific imaginary'.[147] Such imaginaries represent

[144] See, for example: Gartner (2012) *Hype cycles*, available at: http://www.gartner.com/technology/research/methodologies/hype-cycle.jsp. Other models are discussed in Brown N and Michael M (2003) A sociology of expectations: retrospecting prospects and prospecting retrospects *Technology Analysis & Strategic Management* **15**: 3-18.

[145] See: Williams R (2006) Compressed foresight and narrative bias: pitfalls in assessing high technology futures *Science as Culture* **15**: 327-48.

[146] The economist Paul David has argued that 'technological presbyopia' is characteristic of thinking about the microeconomics of biotechnology and other emerging technologies, and accounts substantially for 'productivity paradox': the well-observed phenomenon of fully-realised technologies failing to demonstrate expected impact. He has stated that: "[s]ufferers lose a proper sense of the complexity and historical contingency of the processes involved in technological change and the entanglement of the latter with economic social, political and legal transformations." See: David PA (1989) Computer and dynamo – the modern productivity paradox in a not-too-distant mirror, in *Technology and productivity: the challenge for economic policy* OECD (Editor) (Paris: OECD, 1991), p317. We return to the theme of economic expectations and their influence on public and commercial policy in Chapters 7 and 9.

[147] The phrase 'sociotechnical imaginary' is associated with the work of Sheila Jasanoff (see, for example, Harvard Program on Science, Technology and Society (2012) *The Sociotechnical Imaginaries Project*, available at: http://sts.hks.harvard.edu/research/platforms/imaginaries); others use the phrase to mean the ways in which "dissatisfactions with social reality and desires for a better society are projected onto technologies as capable of delivering a potential realm of completeness" See: Lister M, Dovey J, Giddings S, Grant I and Kelly K (2009) *New media: a critical introduction* (New York: Routledge), p60. For resources on the concept of the 'technoscientific imaginary', see: Harvard Program on Science, Technology and Society (2012) *Imagination in science and technology*, available at: http://sts.hks.harvard.edu/research/platforms/imaginaries/i.ant/imagination-in-science-and-technology.

prospective technologies from particular perspectives that rely on assumptions (which we discuss under the rubric of 'framing' in Chapter 3) drawn from outside technology, for example from cultural traditions and moral commitments. These range from the perspectives of 'transhumanism', to those of groups opposed to the morally 'dehumanising' social consequences of certain forms of technological development,[148] and may be tied up with social and political objectives such as local or national self-sufficiency, or globalisation.

2.35 The sociotechnical imaginaries associated with decision-making processes for biotechnologies are rarely fully, clearly or consistently articulated. This can lead to an obvious problem: where people conceive of and evaluate prospective technologies as elements within their own personal understandings and visions of the future, the possibility of open debate about common social objectives is diminished. This is especially the case where such decision making impinges on the interests of particular individuals or groups. Where these underlying beliefs and understandings are not articulated, general questions about how a technology can improve social conditions may be replaced by questions relating to discrete issues of cost, safety, ease of implementation, usefulness, impact, etc, which appear to have determinate answers, although these 'answers' add up, collectively, to a vision of the future that has not been debated and may be significantly less desirable to some than to others.[149]

Procedural narratives

2.36 The presentation of particular biotechnologies is often set in the context of grander narratives. Synthetic biology has been described as "the third industrial revolution"[150] and references to previous, economically important technologies are offered as precedents to encourage or justify commercial and political investments. For example, a Royal Academy of Engineering report on synthetic biology states that "many commentators now believe that synthetic biology has the potential for major wealth generation by means of the development of major new industries, much as, for example the semi-conductor did in the last century".[151] This alludes to a very common assertion: that while the 20th Century was 'the age of physics', the 21st Century will be 'the age of biology'.[152]

2.37 These grander narratives can be seen mutually reflected in papers and research proposals, science policy documents and science journalism. A notable feature of these narratives is the use of a number of recurring metaphors, many taken from information technology. In discussions of both synthetic biology and stem cell biology, for example, there is frequent appeal to the idea of "reprogramming" cells.[153] The widely publicised experiment referred to above, in which the DNA of a *Mycoplasma capricolum* cell was replaced by an entirely synthetic

[148] Transhumanism (in this sense) is an ideology that valorises the transformation of the human condition through technologies, for example, to promote life extension, cognitive and physical enhancement. See: Bostrom N (2005) A history of transhumanist thought Journal of Evolution and Technology **14**: 1-25. Others see a bias in favour of high technology approaches as technologies as threatening to biodiversity, agriculture and human rights. See, for example, the ETC Group: http://www.etcgroup.org.

[149] A well-known example here is the debate concerning GM crops where (at least during the early stages) the beliefs and approaches underpinning positions on both 'sides' of the debate sometimes appeared obscured, with the public debate itself explicitly focusing on the 'safety' of the crops rather than on the value judgments of the participants (such as the desirability or otherwise of a profit motive, commercial control of genetic resources and views on power dynamics.) See, for example, Wilsdon J and Willis R (2004) *See-through science: why public engagement needs to move upstream*, available at: http://www.demos.co.uk/files/Seethroughsciencefinal.pdf?1240939425, p27.

[150] See: The Royal Society of Chemistry (2009) A third industrial revolution *Integrative Biology* **1**: 148-9.

[151] The Royal Academy of Engineering (2009) *Synthetic biology: scope, applications, and implications* available at: http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf.

[152] The current BBSRC delivery plan opens with a particularly explicit example: "The 21st Century will be the age of bioscience. Driven by new concepts and technologies, a biological revolution is unfolding in the same way that advances in physics shaped the early 20th Century and great leaps in electronics and computing transformed our lives over the past 40 years." See: BBSRC (2011) *BBSRC delivery plan 2011-2015: maximising economic growth in the age of bioscience*, available at: http://www.bbsrc.ac.uk/web/FILES/Publications/delivery_plan_2011_2015.pdf.

[153] Gallivan JP (2007) Toward reprogramming bacteria with small molecules and RNA *Current Opinion in Chemical Biology* **11**: 612-9.

genome,[154] has been described as "rebooting" or "changing the operating system" of life.[155] Its creator has himself been quoted as describing this synthetic cell as "the first cell to have its parent be a computer".[156] Computational metaphors are used when synthetic biologists talk about how DNA can be 'decompiled' through sequencing and then 'recompiled' through synthesis.[157] This metaphor is continued when there is discussion of how in the future biological parts will be combined "in the same manner that Linux modules are now combined to make software".[158] These impressions are only heightened by the conscious adoption of language from information technology, in what might be called biology's 'pop culture', such as the references to 'biohackers' and 'open source biology'.

2.38 For many members of the public, expectations of new technology may arise as much from science fiction, films and video games as from science journalism, a phenomenon known as 'cultivation'. Cultivation analysis has shown how exposure to fictional scenarios in the media can condition expectations of the real world.[159] Themes based on radical genetic modification of organisms, human enhancement and cyborgs are widespread throughout both popular and high culture. However, such influences may not only bear on 'the public': it is interesting to consider to what extent these fictional visions may also be translated back into the world of science. In bionanotechnology, the vision of the 'nanobot' in the form of a miniaturised medical robot has a long fictional pedigree,[160] and it has been argued that many of the themes in 'Plenty of room at the bottom' – the 1959 lecture by Richard Feynman, credited by many as founding the field of nanotechnology – were commonplace in the science fiction of the time.[161] The possibility of using synthetic biology to construct "synthetic ecologies" has been explored in the context of a NASA expedition to Mars,[162] following the familiar science fiction narrative of 'terraforming' uninhabited planets (indeed, in this instance, the term was referenced directly). Meanwhile, the dream of bringing extinct dinosaur species back to life, the central conceit of the novel and film *Jurassic Park*, can be found in synthetic biologists' attempts to resurrect the (albeit much more recently extinct) woolly mammoth.[163]

Methodological scepticism

2.39 While folk narratives and descriptive models may reflect *past* experience, when they are projected into the *future* as a way of organising expectations, they may obscure ambiguities and uncertainties that may be significant for decision making and policy. One uncertainty is that, while expectations of emerging biotechnologies vary over time, they also vary between groups and communities.[164] For example, the detailed technical difficulties and uncertainties that scientists and engineers work with on a day-to-day basis may be invisible to policy makers, investors and the interested public.

---

[154] Gibson DG, Glass JI, Lartigue C *et al.* (2010) Creation of a bacterial cell controlled by a chemically synthesized genome *Science* **329**: 52-6.

[155] See, for example, Katsnelson A (2010) Researchers start up cell with synthetic genome *Nature*, available at: http://www.nature.com/news/2010/100520/full/news.2010.253.html and Perkel JM (2010) *Synthetic genomics: building a better bacterium*, available at: http://www.sciencemag.org/site/products/lst_20110325.pdf.

[156] Jones M (2010) House Committee hears from Venter, others on synthetic biology *GenomeWeb Daily News* 28 May, available at: http://www.genomeweb.com/house-committee-hears-venter-others-synthetic-biology.

[157] Specter M (2009) A life of its own: where will synthetic biology lead us? *The New Yorker* 28 September, available at: http://www.newyorker.com/reporting/2009/09/28/090928fa_fact_specter.

[158] Maurer SM (2009) Before it's too late: why synthetic biologists need an open-parts collaboration—and how to build one *EMBO Reports* **10**: 806-9.

[159] See: Gerbner G (1998) Cultivation analysis: an overview *Mass Communication and Society* **1**: 175-94.

[160] Nerlich B (2005) From Nautilus to Nanobo(a)ts: the visual construction of nanoscience *Journal of Nanotechnology Online* **1**: 1-19.

[161] See: Milburn C (2008) *Nanovision: engineering the future* (Durham, North Carolina: Duke University Press). However, some scientists find this claim controversial. For further discussion, see: Milburn C (2010) Modifiable futures: science fiction at the bench *Isis* **101**: 560-9.

[162] Langhoff S, Cumbers J, Rothschild L, Paavola and Worden SP (2010) *Workshop report on: 'what are the potential roles for synthetic biology in NASA's mission?'*, available at: http://event.arc.nasa.gov/main/home/reports/CP-2011-216430_Synthetic_Bio.v6.pdf.

[163] Associated Press (2008) Scientists close in on woolly mammoth *Los Angeles Times* 20 November, available at: http://articles.latimes.com/2008/nov/20/nation/na-mammoth20; *Crichton M (1991) Jurrassic Park (New York: Alfred A Knopf)*; Spielberg S (dir.) (1993) *Jurassic Park* (film).

[164] Brown N and Michael M (2003) A sociology of expectations: retrospecting prospects and prospecting retrospects *Technology Analysis & Strategic Management* **15**: 3-18.

2.40 More generally, there is a fallacy to be avoided that arises from a tendency to make specific claims for particular emerging biotechnologies on the basis of general premises. One might, for instance, believe that currently emerging biotechnologies will become very important in the future and lead to significant increases in human welfare. But what one needs to know in a decision context is what the benefits and costs of a particular biotechnology are likely to be. The answer to that question cannot be deduced from the likelihood of benefit from biotechnology in general. There is, however, a tendency to conflate the general promise with the specific promise and to use the general promise as a strong reason to promote specific technologies.

2.41 The overwhelming weight of history of technologies is that they do not conform to prior expectations. This is hardly surprising as there are many more ways of things going off track than there are of keeping to plan. Many possible pathways are abandoned at an early stage or crowded out by alternatives. Of these, of course, we have no experience, which tends to support an optimism bias: correct past predictions that are reinforced by the presence of the facts they predict are more likely to be remembered than incorrect ones that never materialised.[165] The technologies in use today perhaps represent that small proportion of possible conjunctions of knowledge, practices, products and applications that have been selected and retained because they have been successful in delivering benefits, although they may also have crowded out even more promising alternatives. Such counterfactual possibilities, as we noted in paragraph 1.17, are difficult to explore from the perspective of the factual history that we inhabit, but it is not 'anti-science' to assert that a proper evidence-based understanding of why new technologies emerge depends on a rejection of the simplistic view that the techniques that have been widely adopted are the only important ones. They are only *part* of the relevant evidence.

2.42 Those biotechnologies that do survive long-term may follow any number of different development profiles. Some may be rapidly diffused, whereas others could develop quietly and steadily. Others may remain 'submerged', making little progress for long periods, or disappearing altogether. (Xenotransplantation, for example, was the subject of considerable experimental and clinical activity during the mid-20th Century but ran into a number of setbacks[166] and, as a consequence, little work was carried out for approximately ten years from mid-1970s onwards,[167] with significant interest only returning around the turn of the present century.[168]) On the other hand, examples of relatively rapid transformative biotechnologies can be found: IVF might be thought of as one such innovation that, despite initially unsupportive conditions,[169] led to the creation of a new and thriving fertility industry.[170]

2.43 The broader perspective we take here recommends a sceptical approach to claims concerning prospective biotechnologies. However, this scepticism is not a cynicism about the long term value of biotechnologies in general or about the wisdom of supporting biotechnology research. It is a methodological scepticism that questions reasoning from experience – or reasoning from an inappropriately selected class of experiences – about the prospective benefits of *particular* biotechnologies. This scepticism questions, for example, projected timescales for technology development that do not take into account the complexity of the material conditions of innovation and the difficulty of the adaptations needed for a new technology to become fully productive. This scepticism is not intended to undermine support for biotechnology research, development and innovation in general, but rather to make it stronger (in the sense of being better founded). The questions it poses are rather about *how much* support should be given,

[165] See, for example, the work of Tversky and Kahneman on judging frequency and probability: Tversky A and Kahneman D (1973) Availability: a heuristic for judging frequency and probability *Cognitive Psychology* **5**: 207-32.
[166] Persidis A (1999) Xenotransplantation *Nature Biotechnology* **17**: 205-6.
[167] Cooper DKC and Groth C-G (2011) A Record of international meetings on xenotransplantation 1988–2010 *Xenotransplantation* **18**: 229-31.
[168] Persidis A (1999) Xenotransplantation *Nature Biotechnology* **17**: 205-6.
[169] See: Johnson MH, Franklin SB, Cottingham M and Hopwood N (2010) Why the Medical Research Council refused Robert Edwards and Patrick Steptoe support for research on human conception in 1971 *Human Reproduction* **25**: 2157-74.
[170] In 1992, when data were first collected on this issue, approximately 14,057 women received IVF treatment in the UK; in 2007 that number was 36,648 after 15 years of fairly steady growth. See: HFEA (2011) *Long-term trends data - patients treated*, available at: http://www.hfea.gov.uk/2585.html.

when compared with other means to further shared social ends; and about how to respond to 'overpromising' or 'overbelieving' in expected outcomes. As such, methodological scepticism is a long-standing feature of reflection on scientific inquiry.

2.44 Of course, methodological scepticism is exacting to both the optimist and pessimist: we should be prepared just as readily to dismiss the likelihood of harms inferred from previous experience as the expectation of benefits. The absence of a good reason to pursue a particular biotechnology trajectory would not constitute a reason for actively resisting it since, by the same argument, we would have no more reason to expect harms than benefits. However, where it is a question of opportunity costs in alternative uses of resources and, potentially, of locking in alternative futures, a more robust manner of choosing is required.

Conclusion

2.45 In this Chapter, we have turned from the achievements, serendipities and unintended consequences of biotechnologies of the recent past to the prospects and vicissitudes of biotechnologies that are currently emerging. Within the fields of nanotechnology, genetic engineering, regenerative medicine and synthetic biology we encounter a mixture of biotechnologies that are in use, in development or that are merely speculative extrapolations of promising scientific discoveries. We noted how expectations about future biotechnologies are influenced by experience, but that this experience is too often drawn from a few successful biotechnologies, sometimes in very different sectors. We argued that great caution needs to be taken when assigning predictive value to such models that simplify the contingencies and non-linearity of emergence and innovation. Visions of an emerged biotechnology are perhaps better understood as functioning as discursive gambits to secure conditions favourable to a particular pathway.[171]

2.46 We have therefore suggested that the correct mode for the appraisal of emerging biotechnologies is a sceptical mode. Such scepticism should not, however, be seen as 'anti-science' but as methodologically responsible. This is for two reasons: first, premature commitment to a technological pathway is likely to be frustrated and could thereby undermine belief in the value of research; second, setting up a particular outcome as a criterion of success, and organising resources and processes around this may miss broader benefits of research or prevent the balanced appraisal of alternatives. This, of course, both leads back into and deepens the dilemma with which we started: it is no longer just about confronting a decision to commit to one technological pathway at a point before sufficient information is available, but rather about how to balance commitments among a potentially large variety of incommensurable alternatives, none of which may appear obviously preferable.

2.47 A task of this Report is therefore to define modes of decision making that avoid the 'foreshortening' and 'tunnelling' that comes of misrepresenting the complexity of the development and innovation context and the possibility of alternative pathways. To do so is to open up new opportunities for ethical reflection that lie outwith dominant narratives linking prospective biotechnologies and social objectives. So far, we have been largely concerned with descriptive questions about the nature and process of emergence and how it is represented. In the next Chapter, we will begin to consider how normative questions of value enter into the governance of emerging biotechnologies.

[171] "Imagined futures help justify new investments in S&T; in turn, advances in S&T reaffirm the state's capacity to act as responsible stewards of the public good. Sociotechnical imaginaries serve in this respect both as the ends of policy and as instruments of legitimation." See: Harvard Program on Science, Technology and Society (2012) *The Sociotechnical Imaginaries Project*, available at: http://sts.hks.harvard.edu/research/platforms/imaginaries.

Chapter 3

The threefold challenge of emerging biotechnologies

Chapter 3 - The threefold challenge of emerging biotechnologies

Chapter overview

In this Chapter we identify three characteristics of emerging biotechnologies that give rise to difficulties in emerging biotechnology governance.

The first of these characteristics is **uncertainty** about whether the desired outcomes can be achieved in practice (or the undesirable consequences avoided). We distinguish the radical uncertainty associated with novel and unprecedented emerging biotechnologies from quantifiable risk, and draw out the consequences of this distinction for rational decision making strategies, concluding that early-stage emerging biotechnologies often require an approach characterised by caution and circumspection.

The second characteristic is the **ambiguity** of meaning and value that can apply to emerging biotechnologies, their objects, practices and anticipated outcomes, whereby different people may value the same outcomes differently, but where each of these different judgments has an equal claim to be weighed in decisions that affect those who make them. We examine the challenge that emerging biotechnologies present to moral categories and the implications of this for moral judgment and consider the significance of ideas of 'naturalness' and 'playing God'. This has further consequences for decision making, in terms of how the meaning of harm and benefit is construed, whose 'harms' and 'benefits' are allowed to count and how these are distributed.

The third characteristic is the **transformative potential** of emerging biotechnologies: the capacity to change the way things are done and to open up hitherto unavailable possibilities. We examine the significance of pervasive technological transformations not only to ways of doing but also to ways of thinking and their consequences for how choices are framed.

We note how the characteristics of uncertainty and ambiguity are managed through the framing of decisions about biotechnologies. We acknowledge that, while framing is indispensible in order to achieve progress, the process may result in the suppression of alternative and important values and perspectives or produce distortions, with potentially significant consequences for social life and welfare.

Introduction

3.1 In this Chapter we identify three distinctive characteristics that make governance of emerging biotechnologies especially problematic. The three characteristics are uncertainty, ambiguity and transformative potential.

- By 'uncertainty' we mean an inescapable lack of knowledge about the range of possible outcomes or about the likelihood that any particular outcome will in fact occur. This seriously limits the possibility of accurately forecasting the consequences of decisions with regard to biotechnologies (positive or negative) and similarly limits the effectiveness of prospective efforts to control these outcomes.[172]

- By 'ambiguity' we mean a lack of agreement about the implications, meanings or relative importance of a given range of possible outcomes, irrespective of the likelihood of their occurrence. Ambiguity reveals the association of different and possibly incompatible meanings and values within the practices, products and consequences of biotechnologies.

- By 'transformative potential' we mean the capacity that some emerging biotechnologies may have to transform or displace existing social relations, practices and modes of production, or create new capabilities and opportunities that did not previously exist, or may not even have been imagined. These outcomes might be entirely unexpected or unsought.

[172] Some characterisations of different aspects of problematic knowledge distinguish lack of knowledge of the likelihoods of each outcome in a known range from lack of knowledge about key characteristics of the range of possible outcomes (e.g. the distinction between 'uncertainty' and 'ignorance' in Stirling A (2007) Risk, precaution and science: towards a more constructive policy debate *EMBO Reports* **8**: 309-15). See also paragraph 3.10. This distinction is entirely consistent with the argument made here, but is not essential in order to convey the key implications on which the present discussion is focused.

3.2 Having explored these characteristics, we discuss their implications for decision making and how, in general, decision making processes cope with them. We will argue that failing to attend to the importance of these characteristics can lead to ethically unsatisfactory decision making.

Uncertainty

3.3 Uncertainty is a state of the mind. It describes a lack of knowledge of the real determinants of future states of affairs. Such determinants may be simply too manifold, complex and interdependent to grasp or we may simply lack the means to observe them.[173] To point to deficiencies of knowledge in this way does not imply any view about what intrinsic indeterminacy may be present in natural processes or technological systems. It only entails that the real determinants of future states of affairs cannot be comprehensively understood.

3.4 Lack of empirical knowledge would matter less if a reliable theory or a well-constructed model were available to guide understanding. It matters a lot, however, in circumstances where a model cannot be relied upon, for example because there are novel or unknown factors in play, or vulnerabilities to 'system effects'.[174] This is not only a matter of uncertainties within the underpinning science but of interdependencies in the innovation system that is necessary for the emergence of new biotechnologies, which involves alignments across science, business, politics and society.

Varieties of uncertainty

3.5 Uncertainty regarding practical outcomes and applications is particularly marked in 'early stage' research and in the development of techniques with an indefinite variety of possible applications. DNA synthesis, for example, has practically unlimited potential uses in a wide variety of fields including health, manufacturing and bioremediation, most of which may not be foreseen at present. For any one of these applications, however, different sets of uncertainties attach to the feasibility of applying the technology and its ability to adapt to the conditions of use. Not all promising technologies are easily translated from prototype to large scale production and not all are enthusiastically adopted by users. In fact, the commercialisation rate of patents is low. Estimates vary but it is likely that by far the greater part of patented inventions are never commercialised,[175] and the drop-off in patent renewal rates is a well noted.[176]

3.6 Identifying examples of prospective technologies that fail at an early stage (before patenting or commercialisation) is inherently difficult due not only to the counterfactual nature of the subject but also because of ambiguity about what constitutes both 'failure' and 'technology' in this context. Failure does not necessarily have to reflect an underlying problem with the technical aspects of the product or technique, but may be attributable to other elements of the material context, such as the economic climate, commercial pressures on the developer, or opportunity costs of development.[177]

---

[173] This complexity may explain both why biotechnologies present distinctive intellectual challenges and why we may be prone to make 'bad' decisions when confronted with problems of the kind presented by biotechnologies. See, for example, Tversky A and Kahnmann D (1974) Judgement under uncertainty: heuristics and biases *Science* **185**: 1124-31. See also: Cilliers P (2002) Why we cannot know complex things completely *Emergence* **4**: 77-84.

[174] I.e. where the interdependency of elements within systems acts as an exponent of small, local effects, potentially leading to global restructuring. The International Risk Governance Council (IRGC) identifies 'systemic risks', where interdependencies act as risk exponents, as one of the sources of 'emerging risks'. International Risk Governance Council (2012) *A characterisation of emerging risks*, available at: http://www.irgc.org/risk-governance/improving-emerging-risk-management-in-industry/a-characterisation-of-emerging-risks.

[175] There is some debate as to the true extent of the commercialisation of patents: Sichelman, for example, notes a number of studies that give figures of non-commercialisation rates between 40 and 90 per cent, depending on a range of factors: Sichelman T (2010) Commercializing patents *Stanford Law Review* **62**: 341-413.

[176] See: Schankerman M (1991) How valuable is patent protection? Estimates by technology field using patent renewal data *The RAND Journal of Economics* **29**: 77-107.

[177] Such reasons were given in 2011 for Geron's withdrawal from the field of stem cell research. See: Pollack A (2011) Geron is shutting down its stem cell clinical trial *The New York Times* 14 November, available at:

3.7 'Successes' may be as hard to predict as 'failures' and examples of welcome serendipity are common in the history of science and technology. As we noted in Chapter 2, the *origins* of invention seem rarely to be found in *plans* for invention and the uses of resulting inventions are often very different from intended uses.[178] The technique of DNA fingerprinting provides an example: although the forensic implications were very quickly realised, the work that led to the development of the technology was concerned with searching for the human copy of the myoglobin gene (which produces the oxygen-carrying protein in muscle).[179] The prevalence of such cases in the history of technology underlines the value of fostering diversity in invention, and accepting uncertainty in the process rather than constraining it to the delivery of predefined objectives.[180]

3.8 Perhaps the most common concern about novel technologies is the difficulty of predicting the likelihood of unintended and undesirable consequences. This both explains and justifies the regulatory burdens that are placed on the introduction of, for example, new medicinal, industrial and agricultural biotechnology products by most governments. Despite these, examples such as asbestos and chlorofluorocarbons (CFCs) provide sobering examples of the difficulties of prediction and the importance of regulatory learning, particularly with regard to effects that accumulate or manifest only over relatively long timescales.[181] The consequences of technological innovation extend into many different dimensions aside from health and environmental impacts. Among the hardest to predict and control, and the longest to accumulate, may be social consequences, that is, the impact a technology will have on the relationships between individuals and groups in the general population. Many of these are only dimly perceived in advance although their effects may be profound, for example: the social consequences of the internet and the World Wide Web,[182] the influence of the motor car on the design of residential areas (especially in the US),[183] or the way in which the availability of the contraceptive pill has changed working practices and the age at which women first give birth.[184] (We return to the question of foresighting of ethical, legal and social implications in Chapter 6.)

3.9 Alongside unintended consequences, uncontrolled uses provide another dimension of uncertainty. The significance of this is exacerbated by the potential of many biotechnologies for so-called 'dual use' (i.e. with both beneficial and harmful applications), often without further adaptation.[185] For example, the knowledge of how to synthesise flu virus may be used to develop vaccines but may equally be used to develop weapons.[186] However the 'repurposing' of

---

http://www.nytimes.com/2011/11/15/business/geron-is-shutting-down-its-stem-cell-clinical-trial.html. However, some have suggested that Geron's overreaching ambition did no favours for the field of therapeutic stem cell research: Boseley S (2011) Geron abandons stem cell therapy as treatment for paralysis *The Guardian* 15 November, available at: http://www.guardian.co.uk/science/2011/nov/15/geron-abandons-stem-cell-therapy.

178 See the classic account in Jewkes J, Sawers D and Stillerman R (1969) *The sources of invention* (New York: WW Norton). For a more recent example, see the apparently inadvertent development of a technique for deriving human embryonic stem cells through parthenogenesis: Mullard A (2007) Inadvertent parthenogenesis *Nature Reviews Molecular Cell Biology* **8**: 677.

179 Newton, G (2004) *Discovering DNA fingerprinting*, available at: http://genome.wellcome.ac.uk/doc_wtd020877.html.

180 The related and important question of when and by what means this diversity should be filtered into desirable innovation pathways – for example, by free markets or other selective mechanisms – is one that we return to later in this Report.

181 For example, the experience of asbestos-related mesotheliomas has encouraged a 'benign by design' approach to the innovations involving carbon nanofibres. (Although the 'benign by design' approach has been at issue in the chemical sciences prior to specifically nanotechnological concerns.) See: Schinwald A, Murphy FA, Prina-Mello A *et al.* (2012) The threshold length for fiber-induced acute pleural inflammation: shedding light on the early events in asbestos-induced mesothelioma *Toxicological Sciences* **128**: 461-70; Newman A (1994) Designer chemistry *Environmental Science & Technology* **28**: 463A.

182 Take, for example, the relatively sudden rise of 'social media' and its influence on the nature of public life. See: Baym NK and Boyd D (2012) Socially mediated publicness: an introduction *Journal of Broadcasting & Electronic Media* **56**: 320-9.

183 For example, the argument that 'urban sprawl' is the result of wide-spread car ownership. See: Glaeser EL and Kahn ME (2004) Sprawl and urban growth, in *Handbook of regional and urban economics, volume 4: cities and geography*, Henderson JV, and Thisse JF (Editors) (Amsterdam: Elsevier).

184 Bailey MJ (2006) More power to the pill: the impact of contraceptive freedom on women's life cycle labor supply *The Quarterly Journal of Economics* **121**: 289-320.

185 Indeed, it has been noted that "all technologies are dual-use. There is no such thing as a technology that cannot be used for evil or malign purposes. Some are closer to weapons, but all of them have that capability". See: Skolnikoff EB (2003) Research universities and national security: can traditional values survive?, in *Science and technology in a vulnerable world: supplement to AAAS science and technology policy yearbook*, Teich A, Nelson S, and Lita S (Editors) (Washington, DC: AAAS), available at: http://www.aaas.org/spp/yearbook/2003/stvwch6.pdf, p69.

186 This led to a voluntary moratorium on the publication of relevant research and a vigorous debate that reached the national media in early 2012. See Box 3.1.

technologies may also be relatively benign and is, in fact, reasonably common, from off-label use of drugs such as 'Avastin'® (bevacizumab) – normally used to treat cancers – to treat the eye condition wet age-related macular degeneration more cheaply than the relevant National Institute for Health and Clinical Excellence-approved drug,[187] to the cosmetic use of neurotoxins such as botulinum toxin (as 'Botox'®).[188] The uncertainties with regard to repurposed technologies are, once again, compounded by ambiguities: one state's 'defence' programme can be construed by another as a threat, for example.[189]

Box 3.1: Repurposing biotechnologies: potential misuse of H5N1 research

Avian influenza (influenza A) is a naturally occurring genus of the influenza virus that is maintained in wild birds but also affects commercial and pet birds and can (rarely) infect mammals. There are multiple sub-types of the influenza A virus which can be divided into viruses of high and low pathogenicity. It is difficult for avian influenza viruses to infect humans, but in 1997 the highly-pathogenic influenza A virus sub-type H5N1 emerged in Hong Kong and transmitted to humans, in some cases fatally. In 2003-4 another outbreak began in south-east Asia; during the period 2003- 2012, the World Health Organization (WHO) recorded a total of 608 cases and 359 deaths.[190] Although H5N1 does not, currently, naturally transmit by aerosol between humans, it remains a major global public health concern as it "might develop the capacity to sustain human-to-human transmission and, thereby, spread worldwide".[191]

Not surprisingly, a great deal of research has been carried out on this virus. In particular, in 2011, two pieces of research ignited "a firestorm of debate".[192] The work, by two separate groups in the US and the Netherlands, contained detailed information regarding alternations of the influenza A H5N1 viruses rendering it capable of mammal-to-mammal transmission by aerosol,[193] and that the relevant mutations were few.[194] The work prompted the US National Science Advisory Board for Biosecurity (NSABB), which was concerned about the 'dual-use' implications of the work (i.e. that the data could allow terrorists to create biological weapons), to recommend censorship of research in this area: delay in publication, redaction of the details of how the virus was modified to allow mammal-to-mammal transmission and observance of a two month moratorium on similar research until the risks were assessed.[195] Although the recommendations of the NSABB are theoretically non-binding, both *Science* and *Nature* (the journals in which the research was to be published) agreed to the delay publication and the scientists involved agreed to a voluntary moratorium.[196] In March 2012, the NSABB concluded that revised versions of the manuscripts by the research groups should be published. Both pieces have now been published.[197]

The original recommendation to delay and redact the papers generated a fierce debate about the conduct and dissemination of dual-use research.[198] Indeed, the entire episode is a good example of how (in this case, potential) uncontrolled use of technologies can influence lines of research and the development of particular technologies: the work highlighted differences in the values different groups applied to the issue and in their approach to calculating potential benefits and harms of a particular technological development. Although such issues are not clear-cut, there was evident (if not surprising) divergence between the scientific community and the security community in terms of the value of openness and transparency, at least during the early stages of the controversy: the WHO argued that "redaction…is not viable";[199] there were "months of wrangling that pitted advisory board against scientists".[200] The principal investigator from the Netherlands noted that "in dual-use research, weighing risks and benefits of the research is the crux…Reaching consensus among scientific disciplines, let alone among the public at large, is virtually impossible."[201]

[187] See: NICE (2010) *Department of Health asks NICE to look into Avastin use for eye conditions*, available at: http://www.nice.org.uk/newsroom/news/DHasksNICEtolookintoAvastinuseforeyeconditions.jsp.
[188] See: del Maio M and Berthold R (2007) *Botulinum toxin in aesthetic medicine* (Berlin: Springer).
[189] Any ostensibly 'defensive' biological weapons research demonstrates this kind of ambiguity.
[190] See: WHO (2012) *Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2012*, available at: http://www.who.int/influenza/human_animal_interface/EN_GIP_20120810CumulativeNumberH5N1cases.pdf.
[191] Briand S and Fukuda K (2009) Avian influenza A (H5N1) virus and 2 fundamental questions *Journal of Infectious Diseases* **199**: 1717-9.
[192] Roehr B (2012) US board says censuring research on avian flu was necessary to prevent a potential catastrophe *BMJ* **344**: e840.
[193] Hayward P (2012) H5N1 research put on hold *The Lancet Infectious Diseases* **12**: 186-7.
[194] Hawkes N (2012) WHO recommends further delay in journals publishing research on bird flu *BMJ* **344**: e1284.
[195] Hayward P (2012) H5N1 research put on hold *The Lancet Infectious Diseases* **12**: 186-7.
[196] Enserink M (2012) Public at last, H5N1 study offers insight into virus's possible path to pandemic *Science* **336**: 1494-7.
[197] Imai M, Watanabe T, Hatta M *et al.* (2012) Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets *Nature* **486**: 420-8; Herfst S, Schrauwen EJA, Linster M *et al.* (2012) Airborne transmission of influenza A/H5N1 virus between ferrets *Science* **336**: 1534-41.
[198] The Lancet Infectious Diseases editorial (2012) Avian influenza and the dual-use research debate *The Lancet Infectious Diseases* **12**: 167.
[199] WHO (2012) *Technical consultation on H5N1 research issues - consensus points*, available at: http://www.who.int/influenza/human_animal_interface/consensus_points/en/index.html.
[200] Hayward P (2012) H5N1 research unleashed, almost *The Lancet Infectious Diseases* **12**: 368-9.
[201] Fouchier RAM, Herfst S and Osterhaus ADME (2012) Restricted data on influenza H5N1 virus transmission *Science* **335**: 662-3.

Uncertainty and risk

3.10 There are significant differences of terminology in the relevant literature regarding knowledge of the future. For the purposes of this Report, we distinguish situations where we face *uncertainty* – where the range of possible outcomes or the relative likelihood of each cannot be determined with reasonable confidence – from situations where outcomes can be characterised and probabilities assigned to them with meaningful levels of confidence. (Some commentators make the further distinction within what we have called 'uncertainty' according to whether the range and likelihood or just the likelihood of possible outcomes cannot be defined.)[202]

3.11 In situations in which outcomes can be confidently characterised and probabilities assigned, quantitative risk analysis may usefully inform decision making. Situations of uncertainty, by contrast, may include 'unknown unknowns' of which we become more aware as technology emerges.[203] In such circumstances, risk analysis is unhelpful and attempts to apply it may be dangerously misleading. The significance of the distinction lies in the possibility of being mistaken about where the limits of our knowledge lie: the relevant distinction is not the conceptual one between uncertainty and risk but the practical one about when awareness of the limits of our knowledge leads us to approach decision making in a different way.

3.12 The decision between 'risk approaches' and 'uncertainty approaches' is actually quite a straightforward matter of confidence in a particular assignment of probability. This may be high, for example, where there is believed to exist a large and long-established body of relevant data, where conditions are expected to remain the same, or where models are fairly robust. Such conditions often apply in areas like well-understood occupational health risks from chemical exposure, the epidemiology of familiar pathogens, or transport safety on long-established infrastructures. Nonetheless, it can often be a matter of judgment as to whether a particular body of knowledge adequately supports a risk approach to a given situation or whether it involves more intractable uncertainty. Such judgments are important for questions of governance: normative theories of decision making distinguish different 'rational' strategies for decisions approached as risk and those confronted as uncertainty, for example, privileging caution over goal-seeking.[204]

Ambiguity

3.13 The second characteristic that we associate with emerging biotechnologies is ambiguity. Ambiguity exists when a single phenomenon is capable of bearing two (or more) incompatible meanings. Unlike uncertainty – which refers to the *impossibility* of determining in advance what outcomes will result from following particular biotechnology trajectories – the difficulty to which ambiguity gives rise is that of reaching a *coherent understanding* or evaluation of the prospects, practices or products of emerging biotechnologies in a way that can support decision making.

---

[202] Our distinction follows that given in Elster J (1983) *Explaining technical change* (Cambridge: Cambridge University Press and Universitetsforlaget). However, Stirling, for example, distinguishes *risk* (outcomes can be identified and probabilities assigned), *uncertainty* (outcomes can be identified but probabilities not confidently assigned), *ambiguity* (the issue is not probabilities – the event in question may already have occurred - but the definitions and interpretations of outcomes) and *ignorance* (there is confidence neither about probabilities nor outcomes). (Stirling A (2007) Risk, precaution and science: towards a more constructive policy debate *EMBO Reports* **8**: 309-15). Tannert, Elvers and Jandrig present a taxonomy based on their 'igloo of uncertainty' which separates open and closed knowledge and uncertainty. (See: Tannert C, Elvers H-D and Jandrig B (2007) The ethics of uncertainty *EMBO Reports* **8**: 892-6.)

[203] Perhaps the most famous description of this was contained in an answer to a question at a press conference given by the (then) US Secretary of Defence, Donald Rumsfeld: "The message is that there are [k]no[wn] 'knowns.' There are thing[s] we know that we know. There are known unknowns. That is to say there are things that we now know we don't know. But there are also unknown unknowns. There are things we don't know we don't know. So when we do the best we can and we pull all this information together, and we then say well that's basically what we see as the situation, that is really only the known knowns and the known unknowns. And each year, we discover a few more of those unknown unknowns." Rumsfeld D (6 June 2006) *Press conference by US Secretary of Defence, Donald Rumsfeld*, available at: http://www.nato.int/docu/speech/2002/s020606g.htm.

[204] For the significance of this judgment for rational decision theory, see, for example: Elster J (1983) *Explaining technical change* (Cambridge: Cambridge University Press and Universitetsforlaget), p185ff.

Ambiguous visions

3.14 In a modern plural society it is almost inevitable that different social groups will have divergent interests and values, and emerging biotechnologies have a particular capacity to polarise these. What look like significant benefits to some (for instance, promises of 'life extension'), may often appear to others, equally reasonably, as worrisome threats (for instance: overpopulation, socially debilitating age profiles, or growing inequality). The issue of whose values and understandings prevail has been taken up forcefully by feminist writing in bioethics.[205] In a democratic society or, indeed, any system that respects the right of individuals and groups to determine their own values and interests, it is an important question how these different understandings of the nature of 'harm' and 'benefit' will weigh in any decision that affects them all.

3.15 Likewise, ideas of what constitutes the *scope* of 'harm' or 'benefit' may differ significantly. For example, the effects of genetically modified (GM) crops may be understood in terms of food safety, environmental impact, global trade, agronomic practice, farmer livelihoods, corporate concentration, property rights, the political economy of food as a whole, or the fundamental relations between humanity and nature. In this example, socially responsible policy making may take into account several of these perspectives; regulation typically considers only the first three – and especially the first.

3.16 A third difficulty lies in determining an ethically and socially fair distribution of these multi-dimensional, differently valued, short- and long-term harms and benefits across different populations or social groups.[206] How much should be gained by particular 'winners' before the impact on specific 'losers' can be justified, if at all, and how should the 'losers' be compensated? How can different valuations be integrated in a decision making procedure? Which, if any, may be set aside? Ambiguity is thus relevant not just to narrow risk-based appraisal of emerging technologies, but also to any notion of ethics-based governance.

Ambiguous practices

3.17 Whereas the ultimate outcomes of emerging biotechnologies may be more speculative, the novelty of practices and products of biotechnologies can be challenging for established forms of understanding or evaluation. This novelty leads to ambiguity about the nature of what is involved in biotechnology, whether it is continuous with previous practice or qualitatively different in some important way (for example, whether and, if so, in what ways, marker-assisted breeding – or induced mutagenesis, or genetic engineering – are importantly different from traditional plant breeding). These ambiguities have been articulated in ways that draw attention to the question of whether biotechnologies involve crossing some 'line' that is invested with ethical importance, and therefore whether the practices involved should be subject to a separate ethical judgment.

3.18 One way in which objections to some biotechnologies have been expressed is through the accusation that practitioners are 'playing God', implicitly crossing a line between forms of agency that are acceptable and those that are improper. Such objections have been levelled, for example, at the creation of an organism with a synthetic genome by the J. Craig Venter Institute. The 'playing God' accusation is one way of expressing unease or dissatisfaction with

[205] See, for example, the articles in *Bioethics* **15**(3),as summarised by the guest editors' note of that edition: Diniz D and Donchin A (2001) Guest editors' note *Bioethics* **15**: iii–v.

[206] See, for example, Beck U (1992) *Risk society: towards a new modernity* (London: Sage); Renn O, Webler T and Wiedemann P (Editors) (1995) *Fairness and competence in citizen participation: evaluating models for environmental discourse* (Dordrecht: Kluwer); Rayner S and Cantor R (2006) How fair is safe enough? The cultural approach to societal technology choice *Risk Analysis* **7**: 3-9.

the apparently untrammelled pursuit of technical advances. As commentators have noted, it may mean different things to different people and stand in for other kinds of concern.[207]

Box 3.2: 'Artificial' life and 'playing God'

In 2010, the J. Craig Venter Institute published in the journal *Science* an article describing how one of its research teams (of which Ventner was a part) were able to design, synthesise and assemble a *Mycoplasma mycoides* genome before transplanting it into a *Mycoplasma capricolum* recipient cell to create new *M. mycoides* cells "controlled only by the synthetic chromosome".[208]

The possibility of creating this kind of cell has prompted a significant amount of commentary on both technical and ethical implications of the work, including a Report of the US Presidential Commission for the Study of Bioethical Issues, published in response to the work at the J. Craig Venter Institute.[209]

Regarding the technical implications, it has been argued that the methods used by Venter and his colleagues allow not only for a search of a minimal organism, but also the ability to "investigate the physiological, ecological, and evolutionary consequences of inserting genes… [with] the potential to engineer large introductions of never-before transferred and unlinked genetic material in synthetic cells… to explore completely novel ecological diversity in bacteria".[210] Venter himself has argued that the work has the potential to usher in "a new industrial revolution".[211]

Ethical commentary on the possibility of creating 'artificial' life has focused in particular on the moral status of relevant organisms and whether or not the creators of such organisms are effectively 'playing God'.[212] Some have argued that the scientists involved were 'playing God' as a consequence of "seeking total and unrestrained control over nature";[213] others note that that they were "'playing God'…much more effectively than earlier genetic engineers…[by] not just tinkering with life, [but] designing and creating it",[214] but also point out that "for many of us, this is not a problem." Other commentators have argued that, notwithstanding the technically impressive nature of the work, the methods used by Venter and his team did not constitute 'creating life'.[215]

Ambiguous objects

3.19 A related way in which biotechnologies may disturb established categories upon which judgments may often rely (at least as a starting place for moral reflection) is through the generation of novel objects. Animals produced by chimerism or transgenesis containing human genetic material,[216] human admixed embryos[217] or embryos reconstructed through mitochondrial transfer,[218] protocells with a synthetic biochemistry not previously seen in nature,[219] extreme

[207] See, for example, Douglas T and Savulescu J (2010) Synthetic biology and the ethics of knowledge *Journal of Medical Ethics* **36**: 687-93.
[208] Gibson DG, Glass JI, Lartigue C *et al.* (2010) Creation of a bacterial cell controlled by a chemically synthesized genome *Science* **329**: 52-6.
[209] Presidential Commission for the Study of Bioethical Issues (2010) *New directions: the ethics of synthetic biology and emerging technologies*, available at: http://www.bioethics.gov/documents/synthetic-biology/PCSBI-Synthetic-Biology-Report-12.16.10.pdf. See also: Thompson PB (2012) Synthetic biology needs a synthetic bioethics *Ethics, Policy & Environment* **15**: 1-20.
[210] Cohan FM (2010) Synthetic genome: now that we're creators, what should we create? *Current Biology* **20**: R675-R7.
[211] BBC News Online (2010) *'Artificial life' breakthrough announced by scientists* available at: http://www.bbc.co.uk/news/10132762.
[212] See, for example, Baertschi B (2012) The moral status of artificial life *Environmental Values* **21**: 5-18; Sandler R (2012) The value of artefactual organisms *Environmental Values* **21**: 43-61.
[213] Dr David King, director of Human Genetics Watch, quoted in Alleyne R (2010) Scientist Craig Venter creates life for first time in laboratory sparking debate about 'playing god' *The Telegraph* 20 May, available at: http://www.telegraph.co.uk/science/7745868/Scientist-Craig-Venter-creates-life-for-first-time-in-laboratory-sparking-debate-about-playing-god.html.
[214] Douglas T (2010) Venter creates bacterium controlled by a synthetic genome on *Practical ethics* [internet blog] 20 May, available at: http://blog.practicalethics.ox.ac.uk/2010/05/venter-creates-bacterium-controlled-by-a-synthetic-genome.
[215] See, for example, Professor Steven Rose writing in *The Guardian*: Rose S (2010) Craig Venter is not playing God yet *The Guardian* 24 May, available at: http://www.guardian.co.uk/science/2010/may/24/venter-not-playing-god-yet. A spokesman for the Vatican argued that, rather than creating life, the experiment simply "replaced one of its motors". See: CNN (2010) *Vatican calls synthetic cell creation 'interesting'*, available at: http://www.cnn.com/2010/HEALTH/05/22/vatican.synthetic.cell/index.html?hpt=T3.
[216] See: Academy of Medical Sciences (2011) *Animals containing human material*, available at: http://www.acmedsci.ac.uk/download.php?file=/images/project/Animalsc.pdf, p70ff.
[217] See: HFEA (2007) *Hybrids and chimeras*, available at: http://www.hfea.gov.uk/docs/Hybrids_Report.pdf.
[218] See: Nuffield Council on Bioethics (2012) *Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review*, available at: http://www.nuffieldbioethics.org/mitochondrial-dna-disorders.
[219] Bedau MA and Parke EC (Editors) (2009) *The ethics of protocells: moral and social implications of creating life in the laboratory* (Cambridge, Massachusetts: MIT Press).

human enhancement and 'transhumanism',[220] and superintelligent computers[221] are all concepts, realised or proposed, that challenge at least some conventional ways of separating objects into categories that are invested with value (organism/artefact; human/non-human; born/made, natural/artificial, etc.)

3.20 The reason that such categories are important is that they often form the basis of moral judgments or the possibility of a system of positive laws. As such, the problems they create may have legal as well as moral consequences where, for example, legal certainty may be necessary in order for research and development of new technologies to progress, or to be brought to a halt definitively. A striking example of this relates to research on cloned or human admixed embryos, which brought about disputes over legal interpretation and debates around enabling legislation.[222]

Taking ambiguity seriously

3.21 There are at least two reasons for taking seriously the implications of ambiguity discussed here. The first is procedural fairness, which includes the requirement that contrary views should not be refused consideration without good reason. Of course, admitting multiple standards of value makes rational decision making difficult. Indeed, long-established findings in rational choice theory[223] show that (especially in a plural society) the notion of a uniquely 'rational' choice for a society is not only difficult in practice but is, in many senses, a contradiction in terms.[224] The second is that failing to take the implications of ambiguity seriously may simply displace or defer the *consequences* of ambiguity. These may then find other forms of expression that may nevertheless influence the emerging biotechnology trajectory in other ways. Such consequences may include the loss of public confidence or trust in particular technological commitments, and also in associated institutions and research disciplines. More widely, the use of narrowly-conceived 'evidence-based' decision making procedures employing methodological formalism but excluding wider societal and political considerations can erode confidence in the impartiality of scientific advice and policy making.[225] Perhaps the most familiar example of this is the experience with GM crops in Europe over the past 20 years. Here, it is widely accepted – including by industry bodies that initially supported the introduction of these products – that the intensity of the public backlash was, in part, due to the exaggeration of the role of science in essentially political matters of technology governance.

---

[220] See, for example, Bostrom N (2009) Why I want to be a posthuman when I grow up, in *Medical enhancement and posthumanity*, Gordijn B, and Chadwick R (Editors) (Dordrecht: Springer), also available at: http://www.nickbostrom.com/posthuman.pdf and Bostrom N (2005) A history of transhumanist thought *Journal of evolution and technology* **14**: 1-25.

[221] In particular, the notion of a 'technological singularity' expressing the overtaking of human intelligence by intelligence not of solely biological origin. See, for example, the influential paper presented by Vernor Vinge in 1993: Vinge V (1993) *The coming technological singularity: how to survive in the post-human era*, available at: http://www-rohan.sdsu.edu/faculty/vinge/misc/singularity.html and Kurzweil R (2005) *The singularity is near: when humans transcend biology* (New York: Viking).

[222] On cloned embryos, see: *R. v. Secretary of State for Health ex p. Quintavalle (on behalf of Pro-Life Alliance)* [2003] UKHL 13; on admixed embryos, see: HFEA (2007) *Hybrids and chimeras*, available at: http://www.hfea.gov.uk/docs/Hybrids_Report.pdf.

[223] Rational choice theory can be considered – at the broadest level – as an attempt to understand behaviour by combining "the advantages of theory-guided research, as found in economics, with the strong empirical tradition of sociology." Lindenberg S (1992) The method of decreasing abstraction, in *Rational choice theory: advocacy and critique*, Coleman JS, and Fararo TJ (Editors) (Newbury Park, California: Sage).See also: Scott J (2000) Rational choice theory, in *Understanding contemporary society: theories of the present*, Browning G, Halcli A, and Webster F (Editors) (London: Sage).

[224] The economist Kenneth Arrow demonstrated the impossibility of any voting system converting the ranked preferences of individuals into a group ranking without simultaneously violating at least one apparently reasonable criterion of fairness. See: Arrow KJ (1950) A difficulty in the concept of social welfare *Journal of Political Economy* **58**: 328-46.

[225] An argument elaborated in Mayer S and Stirling A (2004) GM crops: good or bad? *EMBO Reports* **5**: 1021.

Transformative potential

Technical change and disruptive technologies

3.22 The ways in which new technologies come to be adopted and, eventually, supplant previous technologies has been an important area of theoretical interest to social scientists and, in particular, economists. A number of models have been proposed to explain technology choice behaviour by societies, entrepreneurs and consumers.[226] They offer different explanations of the phenomena of unevenness in technology change (particularly within industry), which tends to be characterised by relatively stable phases during which a dominant technology is in widespread use (and enjoys incremental improvement) and often destabilising transitions to new dominant technological forms. What are now conventionally described as 'disruptive technologies',[227] are novel technologies that are not incrementally linked to existing technologies but that are capable of bringing novel products to market that are cheaper, simpler and more convenient to use than the conventional technologies, or that are capable of developing new markets that did not exist previously.[228] We are therefore concerned with two consequences of technological change (although this distinction is not always clear-cut): first, the ability to perform functions that were already being performed by established technologies but radically more efficiently; second, performing functions that were not possible at all before the appearance of the new technology.

3.23 As shown by the fact that it took over a hundred years to introduce and develop steam engine – perhaps the epitome of a transformative technology – the benefits of transformative technologies may take some time to become established. Perhaps the clearest example of revolutionary technological change (novel technologies becoming pervasive in a short time) is semiconductor-based technologies.[229] However, it may be a mistake to frame our expectations of the pace and linearity of biotechnology innovations by the experience of semiconductors, and even less so our expectations of their measureable impact.[230] The gradient and continuity of innovation is important because it has implications for policy and the profile of resource allocation over time.[231]

[226] Among the most well-known is the 'rational choice' model of neoclassical economics, the 'wave model' associated with Joseph Schumpeter, evolutionary and Marxian models. A helpful survey is provided by Elster J (1983) *Explaining technical change* (Cambridge: Cambridge University Press and Universitetsforlaget).

[227] We consistently prefer the term 'transformative' to 'disruptive'. This avoids any unhelpful negative connotation of the term 'disruptive', but, more importantly, suggests the thoroughgoing way in which novel technologies may reconfigure a domain of dependent possibilities not limited to the economic register.

[228] Christensen CM (1997) *The innovator's dilemma: when new technologies cause great firms to fail* (Cambridge, Massachusetts: Harvard Business School Press).

[229] Semiconductor materials are the basis of transistors, diodes and all integrated circuits and – as such – modern computing.

[230] The increasing computational power of semiconductor technologies is often described as conforming to the famous 'Moore's law', which predicts the exponential rise in the density of transistors that can be placed on an integrated circuit (doubling every two years). Nevertheless, it is not the performance of the technology that is relevant but its conditions of innovation. Paul David makes a related point about the complexity and timescale of economic impacts of technology, reflecting on the quip, attributed to Robert Solow, that "We see computers everywhere but in the economic statistics."

[231] See: Hopkins MM, Martin PA, Nightingale P, Kraft A and Mahdi S (2007) The myth of the biotech revolution: an assessment of technological, clinical and organisational change *Research Policy* **36**: 566-89. The authors conclude: "It may well be better to allocate a greater proportion of resources to other activities, which offer more immediate health gains (e.g., the better adoption of existing 'low tech' technologies with a proven track record of safety and efficacy). Our analysis also undermines the idea that the biotech sector will play a key role in economic growth or regional development through the rapid creation of thousands of new, high-technology jobs."

Box 3.3: The steam engine

The steam engine transformed industrial production in 19th Century Britain, and brought significant improvements to the efficiency of production, as well as extending the possibilities for future products. The steam engine overcame 'hard constraints', making power both portable (based on abundant coal rather than water or wind), and highly efficient (using a highly-concentrated energy source that overcame the hard constraint that limited all previous technologies). This constraint arose from the limits on power density available to previous non-fossil fuel energy sources, which ultimately comes from the rate of arrival of solar power on the earth; preindustrial economies depended on biomass fuel, human and animal power (derived from crops), and renewable sources such as wind and water power (both of which are secondary effects of solar radiation). In comparison to other countries, England was unusual in that the transition to fossil fuel energy happened very early; by 1650, energy from coal already surpassed that of firewood.[232]

However, while the use of coal and steam eventually became pervasive – at least until the arrival of more advanced engines using fossil fuels – it took some time to supplant earlier technologies. This was due to the poor efficiency of steam engines until the late 1800s, combined with the high price of coal as a result of the low technology then applied to its extraction. However, the efficiency of steam power and coal mining improved throughout the 19th Century, and these developments reduced the cost of steam power generally.[233]

Although steam power has arguably become the epitome of a transformative technology, when its impact is measured as a cost/output saving over other sources of industrial power during the early industrial revolution in Britain, it turns out to be much less significant – and less significant for much longer – than its cultural prominence suggests.[234] Long after the innovation of steam engine, however, other technologies continued to advance and to be used alongside it (for example, water power, where water was available as a power source) and, of course, still are. This comparison with counterfactual possibilities rather than with stalled incumbent technologies has been examined by some economic historians, leading to a reassessment of the comparative economic contribution of steam power in specific contexts.[235] Although some of the results of the 'new economic history' are controversial among economists, they point to an important way of posing questions about prospective technologies, taking into account their comparative developmental potential and the importance of the innovation context as well as simple technical superiority.

3.24 By 'transformative potential', we mean something more than simply functional advantage (in terms of speed, cost and efficacy) in achieving certain objectives or extending the range of objectives that can be achieved. Indeed, a technology may be transformative without offering such advantages, that is, it may transform modes of behaviour without making them 'better'[236] at least by some standards. What we mean by transformative potential is the capacity of biotechnologies to supplant existing or alternative modes of practice so thoroughly, that these become marginalised, obscured or even inaccessible. This outcome is a result of the processes of 'lock-in' and 'path dependency' that we have described (see paragraphs1.24 to 1.26 and 1.30 to 1.33), but which, by operating systemically – overrunning both practice and discourse – institutes a new 'paradigm' or technological regime. This regime is one that simultaneously transforms the criteria by which technologies of its kind are evaluated and, eschewing the goals or problems that were the focus of previous regimes, sets new goals and new problems for technology.[237]

3.25 What we are describing, therefore, is a transformation both in ways of *thinking* and in the scope of *practical possibilities* for what we have referred to as the discursive and material contexts

[232] Wrigley EA (2010) *Energy and the English industrial revolution* (Cambridge: Cambridge University Press). By 1850, to meet the energy consumption of England and Wales from firewood would have required almost the whole land area to be forested. This could not have happened, of course, so this level of energy consumption was only possible because that constraint had been lifted through the use of coal.

[233] See: Tylecote A (1992) *The long wave in the world economy: the current crisis in historical perspective* (London: Routledge), pp36-70.

[234] Von Tunzelmann N (1977) *Steampower and British industrialisation to 1860* (Oxford: Oxford University Press).

[235] See, for example, analyses in the vein of the 'new economic history' pioneered by Robert Fogel. Fogel reassessed the comparative impact of steam railways to the transportation of agricultural products in the US in the 19th Century to a few percentage points of gross domestic product; see: Fogel R (1964) *Railroads and American economic growth: essays in econometric history* (Baltimore, Maryland: Johns Hopkins University Press). See also: Fogel RW (1966) The new economic history: its findings and methods *Economic History Review* **19**: 642-56.

[236] Such as the 'rational design' approach to drug discovery. See: Hopkins MM, Martin PA, Nightingale P, Kraft A and Mahdi S (2007) The myth of the biotech revolution: an assessment of technological, clinical and organisational change *Research Policy* **36**: 566-89. See also Chapter 1.

[237] The notion of a 'technological paradigm' was developed in technology studies literature to support evolutionary explanations of both continuous and discontinuous technical change, notably by Giovanni Dosi (see: Dosi G (1982) Technological paradigms and technological trajectories: a suggested interpretation of the determinants and directions of technical change *Research Policy* **11**: 147-62). Most definitions in the literature imply, saliently, that the paradigm defines the domain of what counts as a relevant or important problem, even to the extent of obscuring and excluding appreciation of other problematics.

(see paragraphs 1.19 to 1.23). Frequently, the discursive transformation may pre-empt the material transformation. This does not mean that pervasive benefits should not be expected from the currently forecast 'revolutions' in biotechnology. Nor, importantly, does it mean that this present discourse of transformation will have been inconsequential in relation to whatever transformations may occur in future. Indeed, it may have a significant effect, which is why we argue that special attention should be given to this discourse. What we must attend to in developing an ethics of emerging biotechnologies, and what our methodological scepticism questions, is the possibility of research and innovation being caught up in an anticipatory paradigm, one that shores up the 'biotechnology wager', by committing particular social objectives to biotechnological solutions and, in some cases, to particular prospective technologies.

Framing emerging biotechnologies

3.26 The characteristics of emerging biotechnologies we have discussed appear to bring us to a point of more fundamental scepticism. Uncertainty and ambiguity undermine the rational bases for decision making. How, after all, can a decision be made about what conditions to put in place in order to support a biotechnology – or biotechnology generally – if one cannot determine the likelihood of it providing a benefit that is sought or if one cannot be sure that what is sought is even a benefit at all? How can the value of alternatives that exist outside the paradigm that circumscribes value be considered? Yet conditions such as funding, institutions, and regulatory procedures, are routinely put in place, apparently in the aid of realising sometimes very specific outcomes from technological initiatives. We now examine how uncertainties and ambiguities may be managed, and, in the next Chapter, identify the elements of an ethical approach to doing so.

The idea of a 'frame'

3.27 Decisions about the conditions that influence the direction of biotechnology research, development and innovation arise in different contexts. However, all emerge against a background of knowledge, beliefs and values that give a particular significance to different possible options. Arguing for one set of conditions against another implicitly or explicitly invokes this background as a reason for preferring it to the available alternatives. We describe this background as a 'frame'.[238] For instance, a firm may think of funding the development of a new product because it has expertise in that area and believes it can return a profit, but its criteria may be limited to those that are relevant to the market, and not, for example, the social impact of the product. That product may privilege a particular range of consumers or produce a comparative disadvantage for others. How those consumers see the product may, on the other hand, depend very much on those factors.

3.28 Frames may be coextensive with more or less coherent technical perspectives (for example, academic disciplines or particular paradigms within – or transecting – these). Individual actors may approach decisions by first, perhaps unconsciously, selecting an appropriate frame through which to interpret the phenomena in question.[239] While frames may be connected with, and determine, the quality of individual subjective experience, we use this concept in this Report to denote a phenomenon of public discourse rather than individual psychology. Thus one frame may be shared by a number of people and one person may interpret a single phenomenon in a variety of ways depending on the frame that they apply to it.

3.29 Framing is indispensible to understanding the social meaning of biotechnologies, as it is to the understanding of any social phenomenon: it responds to the complexity of facts and values in play by filtering, organising and ascribing relevance to them. Two important considerations lie

[238] The sociological concept of the frame derives from the work of Goffman; see: Goffman E (1986) *Frame analysis* (Boston, Massachusetts: Northeastern University Press).

[239] This question of attaching meaning to social phenomena is the one with which Goffman initiates his inquiry: "I assume that when individuals attend to any current situation, they face the question: "What is it that's going on here?" Whether asked explicitly, as in times of confusion and doubt, or tacitly, during occasions of unusual certitude, the question is put and the answer to it is presumed by the way the individuals then proceed to get on with the affairs at hand." (p8.)

behind this: firstly, a frame is always necessary to give phenomena significance; secondly, there is no 'universal' or 'absolute' frame that would synthesise every possible meaning or value. From this it follows that all frames are incomplete, that alternative framings are always possible, and that it is rarely self-evident that any one frame should be privileged over alternatives.

3.30 Nevertheless, in relation to many familiar social phenomena, specific aspects of frames may be well-established and widely shared. For example, in a society with common cultural and religious traditions, and commitments to human rights, common value frameworks contribute to making the everyday behaviour of individuals relatively consistent and predictable, within certain limits. If it were not for the way that frames are embedded in public discourse, a pernicious relativism might be inescapable. Consistent moral frames also allow a given individual to make consistent choices over time and – importantly – to assimilate novel phenomena.[240] However, frames are also dynamic; whatever their innate conditions of possibility, they are subject to reconfiguration and learning in response to novel challenges.

3.31 The importance of considering alternative frames in the governance of emerging biotechnology is heightened by the fact that so many social processes operate in the real world effectively to 'close down' the plurality of frames that may be applied. These processes are often typical of routine decision making processes where institutional bias or 'groupthink' are found.[241] This does not imply that alternative frames may not coexist with the dominant frame, or only that they are not 'granted' equal status to influence outcomes.[242] Governance processes that do not effectively mitigate such pressures may foreclose the range of frames through which emerging biotechnologies are understood and evaluated. Evidence-based policy making, often concerned with formalised assessment of impact and risk, is a common mitigation but, as we argued in Chapter 1,[243] with emerging biotechnologies there are significant difficulties in applying evidence, a conclusion that has led to our more sceptical and reflective approach. In the next two sections, we describe the role of frames in suppressing the uncertainty and ambiguity associated with emerging biotechnologies.

Uncertainty reduced to risk

3.32 As we have argued above, one convenient simplification effected by framing is to bring phenomena subject to uncertainty and ambiguity within a context that supposes the possibility of a rational preference. As a consequence, decisions may be guided by a misplaced confidence in the relevance of an evidence base, risk management methodology and quantification. Likewise, the significance of ambiguity may be repressed through social processes of aggregation and consensus.

3.33 However, even at the limit of full confidence in the identification of outcomes and the assignment of likelihoods of each, it has been shown that decision making is not immune from the effects of presentation, manipulation of language, individual psychology and group dynamics.

3.34 The findings of psychological research have shown that human subjects, when confronted with risk, make choices that are not consistent with calculative rationality,[244] that the framing of choices tends to affect this in certain ways and, in some cases, that the 'framing effect' can be

[240] See: Plous S (1993) *The psychology of judgment and decision making* (New York: McGraw-Hill).

[241] For example, the methods by which the Royal Air Force prosecuted its bombing campaign during the Second World War, or the interpretation of intelligence relating to weapons of mass destruction during the lead up to US-led invasion of Iraq in 2003. See: Edgerton D (2008) *The shock of the old* (London: Profile), p13-4 and US Select Committee on Intelligence (2004) *Report of the Select Committee on Intelligence on the U.S. intelligence community's prewar intelligence assessments on Iraq, together with additional views*, available at: http://www.intelligence.senate.gov/108301.pdf, p18.

[242] This does not imply any deliberate intention to dominate or mislead. It may come about, for example, by means of individual prejudice, selective resourcing, expedient design, organisational incentives, economic interests, and associated patterns of advancement, preferment and patronage.

[243] See Box 1.2.

[244] See the work of Tversky and Kahneman, discussed in paragraphs 2.41, 3.3 and 4.13.

measured. They do not show that framing effects are consistent or universal.[245] However, they do demonstrate a malleability in human agents faced with complex situations that is sufficient to conclude that framing has a significant, if not wholly predictable or reproducible, effect.

Box 3.4: Framing effects

Research on the influence of psychological factors on the outcome of decisions made under determinate risks noted how, when the same facts were presented to research subjects in different ways, and all other things being equal, their choices tended to be influenced by the mode of presentation.[246] The authors noted that it is a common pattern that choices presented as possible gains produce risk-averse decisions, where as choices presented as possible losses produce risk-taking decisions, whether those losses or gains are in terms of money, time or human lives lost or saved. The difference between these outcomes is explained as the 'framing effect'.

In one of the most frequently cited examples, when research subjects were presented with alternative preparations for an outbreak of 'an unusual Asian disease' that was expected to kill 600 people, when the alternatives were presented in terms of lives saved a significant majority chose the certain gain (200 lives saved) over the more risky option (1/3 probability that 600 people will be saved and 2/3 probability that 600 people will die), even though it represented an equal expected value. However, when the same choice was presented in terms of lives lost a similarly significant majority chose the more risky programme (1/3 probability that nobody will die and 2/3 probability that 600 people will die) over the certain loss (400 deaths).[247]

The authors identified a number of psychological phenomena that are relevant to decisions under uncertainty and the way in which we use evidence. Their 'availability heuristic', for example, may explain the point made in Chapter 1 about the optimism bias that arises as a result of examples of successful technologies being more available to recall than failed ones.[248]

Ambiguity reduced to univocality

3.35 Another effect of framing is to limit the dimensions of ambiguity by restricting the range of different types of relevant consideration. Thus, if a question to be determined is considered to be a purely technical matter, choices will be focused on the best way of meeting technical standards rather than other kinds of normative standard.[249] This may mean, for example, that the collateral or long term costs are not adequately represented, or unintended consequences are not adequately considered. In contexts framed by economic values, long term social consequences may also receive little consideration. If economic activity is a poor proxy for the welfare of populations, encouraging entrepreneurialism and commercial activity offers no guarantee that public interests will be served. Nevertheless, there is abundant evidence, particularly since the economic downturn, of a foregrounding and privileging of economic framings in research policy.

3.36 The dominance of a particular technological paradigm also limits consideration of alternative technological pathways that may offer a different, but equally feasible, mix of costs and benefits. Where the set of criteria of 'success' of the technology progressively adapts to the actual outcomes of research, feedback between the discursive determination of criteria for 'technological success' and the material conditions of technological progress becomes self-reinforcing and self-justifying.[250]

Conclusion

3.37 The uncertainties and ambiguities of emerging biotechnologies, and their potential to transform not only methods of production and the range of things produced but also ways of thinking and

[245] Druckman JN (2001) Evaluating framing effects *Journal of Economic Psychology* **22**: 91-101.
[246] Tversky A and Kahneman D (2007) The framing of decisions and the psychology of choice *Science* **211**: 453-8. The paper concludes: "When framing influences the experience of consequences, the adoption of a decision frame is an ethically significant act."
[247] Ibid.
[248] See Tversky A and Kahneman D (1973) Availability: a heuristic for judging frequency and probability *Cognitive Psychology* **5**: 207-32 and other works by those authors referred to in paragraphs 2.41, 3.3 and 4.13.
[249] For example the way in which "FSA policy is determined only by sound science" in relation to genetically modified foods: see BBC News Online (2010) *Academic quits GM food committee*, available at: http://www.bbc.co.uk/news/10229106.
[250] Collingridge describes this as the *conservation of technology* effect (Collingridge D (1980) *The social control of technology* (Milton Keynes: The Open University Press), p139); Rip's promise-requirement cycle exhibits a similar dynamic.

valuing, argue that there is a need for a more sceptical and reflective approach to the framing of decisions that shape their emergence. When we think about emerging biotechnologies, it is important to think about *how* we think about them. The challenge of uncertainty and ambiguity does not mean that there can never be a basis for distinguishing better options from worse. It is not framing itself that is the problem, since it is indispensible, but *how* decisions are framed in terms of the kinds of normative questions that are treated as most important. The framing of decisions is especially important in emerging biotechnologies in light of the need to manage high levels of uncertainty and ambiguity.

3.38 Economics and wider social science offer insights into specific mechanisms through which real-world markets and institutions can readily end up favouring technological options that are manifestly problematic and may even be economically suboptimal. More insidiously, the pursuit of technical or economic standards may favour technologies that entrench and even widen social divisions. It matters, therefore, that we recognise the uncertainties involved in governing biotechnologies, and that we approach them not with a misplaced confidence in calculated risks and benefits, but with caution and circumspection, and set within the broader context of social values and objectives.

Chapter 4

Public ethics and the governance of emerging biotechnologies

Chapter 4 - Public ethics and the governance of emerging biotechnologies

Chapter overview

In this Chapter we argue that the nature and potential of biotechnologies suggest that there is a significant public interest in emerging biotechnologies. This arises from a number of sources, including their capacity for public benefit and harm, the public resources invested in them and the collective action such support requires, the peculiar features of the use of living systems, and their potential to transform and 'lock in' social relations and forms of discourse.

There is a *prima facie* ethical reason to support biotechnology research in general, namely, the potential of that research to provide public benefits. However, the uncertainty that any particular line of research will produce expected benefits, coupled with the opportunity cost of pursuing that line of research to the neglect of others – particularly where those other lines of research promise benefits that might be valued more highly by others – suggests that there is a both a strong public interest in the governance of emerging biotechnologies and that the public interest varies, depending on which 'public' we are examining.

We argue that biotechnology governance should be guided by a notion of public good that invokes a 'public ethics'. This is different from individualistic ethics that attempts only to protect the freedoms of individuals in ways compatible with the freedoms of others within a society in that it recognises that a choice must be confronted as one that, to some extent, determines the conditions of common social life.

We argue that governance of emerging biotechnologies in which there is a strong public interest, particularly those that are (potentially) socially transformative, should therefore be subject to a public discourse, that is, subject to a public rather than a private negotiation that is dominated by a particular discipline or interest (or conjunction of disciplines or interests). This public governance should be carried out through an 'engagement' that is cultivated though virtues that serve to ensure that the public interest is expressed.

It is through this construction of a public discourse on emerging biotechnologies that governance conditions can be determined in relation to the public good, through an interrogation of contrasting imaginaries associated with different technologies and how these involve and express substantive values including, equity, solidarity and sustainability.

Introduction

4.1 So far in this Report, we have been concerned largely with biotechnologies as means to putatively desirable ends, although we have noted considerable space for argument both about the relative desirability of those ends and the likelihood of biotechnologies – either in general or particular – bringing them about. This has led us to adopt a sceptical approach to assessing the foundation of expectations about the prospects and timescales for promised benefits of biotechnology. We found that – where there is a deficit of relevant evidence supporting these expectations – this is often made good by features of discourse. This, in turn, has led to our conclusion that there is a need to interrogate the framing of decisions about committing material support to particular biotechnology pathways in order to appreciate and respond to uncertainties and ambiguities. Opening the framing in this way sets such commitments in the context of opportunity costs and alternative pathways. This is important because there is a danger that some social objectives may be 'captured' by a particular research programme and marked out as 'biotechnology' objectives.

4.2 We will argue in this Chapter for a distinctive 'public ethics' of biotechnology governance. Our argument has four parts: first, that there is a distinctive public interest in biotechnology governance; second, that this interest has an ethical dimension but one that may not be unified or necessarily discoverable through reason; third, that features of the policy and innovation system often act to frame and limit the full expression of this interest and, fourth, that this interest may be restored through a particular discursive approach to policy making and governance, reintegrating biotechnology governance with the broader exercise of social interests.

Public interest and the public good

Sources of public interest

4.3 It is often claimed that technologies in themselves are morally neutral, that it is the uses to which they are put and the intentions of those who use them that are morally relevant. This argument could be made about practically any technology. Arguments of this sort are usually deployed to support individual and commercial freedoms and to defend them from the encroachment of social values. While there may be private interest in developing biotechnologies, whether for commercial or other reasons, it is evident that, depending on the possible applications, there is almost certainly a public interest in biotechnologies, although this is not necessarily of a unified nature. So we may ask what distinctive features might make biotechnologies a matter of public interest in our society rather than private interest.

Public benefits and harms

4.4 The first of these distinctive features derives from the fact that the potential benefits and harms to which biotechnologies give rise may be of a public nature. We all share an interest in living in an environment that is conducive to our health and welfare, and having access to affordable food, health care and sustainable energy resources. Some of these are goods from which everyone benefits directly, such as environmental amelioration or the avoidance of impending harms such as pandemic disease. Others might be goods that everyone benefits from having them available, should they need them.

4.5 Potential harms may also be public harms, either direct (e.g. the accidental release of an engineered pathogen) or indirect (e.g. exacerbated social inequality). In some cases, biotechnologies may be different from other technologies in that their effects are mediated through complex biological and ecological systems that may have widespread, exponential (owing to system effects), or long term consequences. While not necessarily of greater magnitude or longevity than the adverse effects of other technologies (a nuclear accident, for example), the complexity of the biological systems in which they operate, and the obscurity of the effective mechanisms, can make these effects harder to envisage, predict and to control.

Public goods, and the fair and effective use of public resources

4.6 If 'biotechnologies' can be understood as conjunctions of knowledge, practices, products and applications, the goods thus bound together are conceptually distinct and may occur separately in practice. Knowledge, in particular, is a good that economists conventionally describe and treat as a 'public good', not in the sense of being 'good for the public' but in the sense of a commodity having certain characteristics that make it difficult to trade through private transactions. A public good is conventionally defined as a good that is *non-rivalrous* or *non-excludable*, or both. A good is non-rivalrous if my use of it does not in any way reduce the amount of it available for you to use. (So, for example, a musical performance is a non-rivalrous good because my enjoyment of it does not diminish your ability to enjoy the same performance.) Scientific knowledge is a public good in this sense because it may be put to use without being 'used up' in the process. Scientific knowledge may also exhibit the characteristic of being non-excludable. A good is non-excludable if it cannot be made available to you without also making it available to me and any number of others who might also wish to enjoy it. (The musical performance could be made excludable by selling tickets, so that those who have not bought tickets will not be admitted to the auditorium. The light from a street lamp or from a lighthouse, on the other hand, is generally regarded as a non-excludable good.[251]) Non-excludability

[251] Of course, it is possible to imagine street lighting being provided via commercial subscription by residents in a particular area while others may still always make use of the resource by 'free riding'. However irksome the free-riding, the subscription system could survive because the use of the good is of value to those who have paid and non-rivalrous (although a tipping point may be reached if the streets become overly congested by light seekers, street traders, etc.).

sometimes gives rise to what is known as the 'free rider' problem, where people enjoy for free a good that others have borne the cost of providing.[252] Thus, once a contribution to scientific knowledge becomes widely known, it is not possible to prevent anyone with a certain level of scientific understanding from learning about it and making use of it.

4.7 Some of the goods bound together in biotechnologies may be regarded as private and others as public. In contrast to the knowledge component, the product component of biotechnologies may very well be both rivalrous and excludable, and therefore a marketable good. (This is irrespective of whether it is a good, like vaccines or other medicines, whose wide availability is socially desirable to the extent that it is provided by the state and funded through general taxation). For example, biofuels, pharmaceuticals, medical treatments, genetically engineered seeds and animals may all be bought and sold at a price determined by the market (although their desirable characteristics may attract subsidies and other interventions, just as undesirable ones may attract regulatory burdens and other penalties). On the other hand, some biotechnology products are non-excludable. These include goods such as bioremediation (dealing with oil spills, for example) or environmental amelioration.

4.8 Public goods typically require collective will and collective action to deliver.[253] Because of the absence of an adequate commercial incentive to develop public goods, they are generally provided by governments (or charities), either through the public sector providers or through purchasing from private providers funded by general taxation. In the case of some goods, such as national prosperity through innovation and military strategic advantage, the relevant collective may be equivalent to a national political jurisdiction. However, there is an argument – based on the fact that there are strong bonds and interests that cross national borders (the shared experience of, and interest in, climate change or pandemic disease, for example) – that some biotechnologies may belong to a special class of 'global public goods'. These are goods that "tend towards universality in the sense that they benefit all countries, population groups and generations".[254] Examples might include scientific and practical knowledge, and 'global policy outcomes' such as global health benefit sharing or bioremediation.[255]

4.9 Given that at least *some* component elements of biotechnologies are public goods requiring collective action, a further source of public interest is in the considerable quantity of public resources that are invested in generating them, for example, the funding of knowledge generation through academic research councils and in higher education, and various public schemes to support biotechnology science and innovation. Such funding is invested in the expectation of a return that will make a positive contribution to the good of the nation and, indeed, beyond, in terms of direct benefits within biotechnology sectors – such as health care and agriculture – and often, more prosaically, to national income generally.[256] It is this expectation that we expressed through the shorthand of the 'biotechnology wager'.[257] There is therefore a public interest that public resources are invested wisely and distributed fairly, and used in accordance with other public values.

The value of living things

4.10 In addition to the interest that people have in biotechnologies as means to further ends that are desired, a further set of ethical interests in the nature of biotechnologies themselves must also

[252] For an overview of the free rider problem, see: Hardin R (2003) The free rider problem *Stanford Encyclopedia of Philosophy*, available at: http://www.science.uva.nl/~seop/entries/free-rider.
[253] Olson M (1965) *The logic of collective action: public goods and the theory of groups* (Cambridge, Massachusetts: Harvard University Press).
[254] Kaul I, Grunberg I and Stern M (Editors) (1999) *Global public goods: international cooperation in the 21st Century* (New York: Oxford University Press). See also: O'Neill O (2011) *Broadening bioethics: clinical ethics, public health and global health*, available at: http://www.nuffieldbioethics.org/sites/default/files/files/Broadening_bioethics_clinical_ethics_public_health_&global_health.pdf.
[255] We look at ways in which these various goods are provided in Chapters 7 and 9, where we discuss issues of national research and innovation policy, and commercialisation, respectively.
[256] Although, as we note elsewhere, increased economic activity does not necessarily entail social benefits. See paragraph 9.31.
[257] See paragraphs 1.1 to 1.3.

be considered. These ethical interests are not about valuing biotechnologies only in terms of the outcomes they may bring about, but rather about valuing the practices they involve and what these mean for the individuals who take part and the society in which they take place. What is most distinctive about biotechnologies among technologies more generally is the implication contained in the prefix 'bio', namely that they utilise or affect living things including, therefore, ourselves. The significance of this distinction between technologies applying to inert matter and those applying to living things is, however, notoriously difficult to pin down.

4.11 For certain religious faiths, this intuition is consistent with injunctions codified in 'revealed' systems of ethics. These may attach distinctive kinds of importance to specific living things, and include, for example, prohibitions on treating them in certain ways. For example, where traditional Christian ethics tend to subordinate animals to human ends without moral consideration, Judaism and Islam both forbid causing pain to animals or hunting for sport, and Judaism has prescriptive rules about the production of food crops.[258] These have had to be successively reinterpreted in the modern scientific age in light of, for example, developments such as the *in vitro* creation and manipulation of embryos or the genetic engineering of plants. Such injunctions may often accord with the intuitions of folk morality regarding the treatment of complex and, especially, sentient beings that appear to exhibit autonomy in the way that non-living systems do not.[259]

4.12 Different cultures and religions have found ways of ordering living beings so as to express their relative importance but also, significantly, their continuity as a class (i.e. the relatedness, by intermediate steps or degrees of genetic similarity, of all living beings). The 'great chain of being' developed in medieval Christianity, for example, with God at its head and other beings arranged in descending degrees of perfection, has its roots in Plato and Aristotle; Darwinian evolution, and modern genetics similarly emphasise both continuity and difference in their theories of descent and inheritance. The distinctive autonomy of living beings is apparent in the often complex ways in which living things interact with and transform themselves and their environment, and by their powers of reproduction, allowing natural purposes – or 'ends' – to be imputed to them. Notions of a natural order, harmony and ends are deeply engrained in almost all cultures and bind groups and societies powerfully together. The term 'the wisdom of repugnance' has been coined to evoke and enjoin a shared sense of distaste for certain biotechnological practices that appear 'contrary to nature' in this sense.[260]This notion is close to what, from a less sympathetic perspective, is often referred to as the 'yuck factor'.[261] Where such sentiments are widely shared they can form a powerful basis for moral restraint and, indeed, for positive legislation[262]; however, where there are moral disagreements, moral arguments can quickly reach an impasse (since my sentiment towards a given action does not logically contradict your different sentiment).

---

[258] See, for example, Brunk CG and Coward H (Editors) (2009) *Acceptable genes? Religious traditions and genetically modified foods* (New York: State University of New York Press).

[259] Different cultures have found ways of ordering living beings in a way that expresses their relative importance but also, importantly their continuity as a class (we are related by intermediate steps to all other living beings). The 'great chain of being' for example, has its roots in Plato and Aristotle but was a conspicuous feature of Neoplantonism and medieval Christianity, among other movements. Darwinian evolution and modern genetics similarly emphasise both continuity and difference in their theories of descent and inheritance.

[260] Kass L (1997) The wisdom of repugnance *The New Republic* **216**: 17-26, reproduced and available at: http://www.catholiceducation.org/articles/medical_ethics/me0006.html.

[261] As JBS Haldane remarked in *Daedalus: science and the future*: "There is no great invention, from fire to flying, which has not been hailed as an insult to some god. But if every physical and chemical invention is a blasphemy, every biological invention is a perversion. There is hardly one which, on first being brought to the notice of an observer from any nation which has not previously heard of their existence, would not appear to him as indecent and unnatural." Haldane JBS (1924) *Daedalus, or, science and the future: a paper read to the Heretics, Cambridge, on February 4th, 1923* (London: EP Dutton), reproduced and available at: http://cscs.umich.edu/~crshalizi/Daedalus.html.

[262] "[P]eople generally want some principles or other to govern the development and use of the new techniques. There must be some barriers that are not to be crossed, some limits fixed, beyond which people must not be allowed to go. Nor is such a wish for containment a mere whim or fancy. The very existence of morality depends on it. A society which had no inhibiting limits... would be a society without moral scruples. And this nobody wants." Committee of Inquiry into Human Fertilisation and Embryology (1984) *Report of the committee of inquiry into human fertilisation and embryology*, available at: http://www.hfea.gov.uk/docs/Warnock_Report_of_the_Committee_of_Inquiry_into_Human_Fertilisation_and_Embryology_1984.pdf, paragraph five. This report led to the UK's Human Fertilisation and Embryology Act 1990.

4.13 Even setting aside shared attitudes to the treatment of particular living things (albeit that, in a plural society, there will inevitably be marginal or 'grey' areas) there is an even more immediate shared interest in living systems generally, given that, as human beings, we interact with and depend on such systems, both individually and collectively. The environmental movement has drawn attention to the complexity and fragility of ecosystems and humanity's interdependence with them, prompting concerns that technological interventions are occurring too quickly, before their consequences can be understood,[263] or even that human understanding in science and technology are not sufficiently sophisticated to intervene in complex natural systems. It has also been argued that such interventions risk destabilising sensitive natural equilibria in a way that may lead to catastrophic consequences (such as climate change). A strong version of this concern suggests that there may be particular limits to human cognition such that it is inadequate to master high-order natural complexities, and that we instead frame or simplify them in conventional, if not arbitrary, ways that may give rise to severe errors in judgment.[264]

4.14 Although natural systems themselves present significant threats to humans (through, for example, plague, famine, floods and tempests), the ability to exercise new kinds of voluntary control over natural processes using the instrumental power of modern biotechnology adds a novel set of issues in which there is clearly a public interest, setting aside whether or not such control can be exercised effectively. These include questions about who exercises such control, their motives, and the quality of their judgment. There may be questions of accountability and vested interest concerning the motives of particular scientists, private firms or public research sponsors, advisors or governments. There may be questions about the dominance of technology within social and cultural change more generally, connected with an interest in ensuring that science and technology do not advance ahead of social and cultural understanding (i.e. because such understanding is an important enabler of technology governance), and with the related fear that, if they do, the dominance of a technological perspective may lead to a 'slippery slope' where ethical control of technology loses its purchase. All of these concerns involve questions about how people act within a shared physical, social and global environment and, in particular, the relationship between science and technology and social, cultural, religious, and other dimensions of life.

Technological determinism

4.15 These interests are intensified by the consideration that social and political commitments to biotechnology often necessarily involve opportunity costs and may create potential path dependencies and irreversibilities. A technology that possesses transformative potential will potentially affect a great many, if not most people. All of these people may have a legitimate interest in being involved in shaping exactly which of the many possible transformations are to take place. More insidious, however, is the potential of biotechnologies to determine the horizon of possibilities for society in a non-trivial way,[265] that is, that the technologies in use exert a dominant or shaping force on society and social organisation.[266] Indeed, it has been argued by some that the larger and more complex technological systems become, the more they tend to shape society and the less amenable they are to being shaped by it.[267]

---

[263] This is an environmental analogue for the social concerns expressed in the 'Collingridge dilemma' – see paragraphs 1.27 to 1.29 and Box 1.2.

[264] A strong version of this concern suggests that there may be particular limits to human cognition such that it is inadequate to master high-order natural complexities, and that we instead frame or simplify them in conventional, if not arbitrary, ways that may give rise to severe errors in judgment. As noted previously, see the work of Amos Tversky and Daniel Kahneman for a discussion of the nature of human decision making: Tversky A and Kahnmann D (1974) Judgement under uncertainty: heuristics and biases *Science* **185**: 1124-31; Kahneman D and Tversky A (1979) Prospect theory: an analysis of decision under risk *Econometrica* **47**: 263-91; Tversky A and Kahneman D (1981) The framing of decisions and the psychology of choice *Science* **211**: 453-8.

[265] A nation becoming a 'knowledge economy', a 'biotech economy', for example. See also: Brinkley I (2008) *The knowledge economy: how knowledge is reshaping the economic life of nations*, available at: http://www.theworkfoundation.com/assets/docs/publications/41_ke_life_of_nations.pdf, p12. "

[266] See: Winner L (1978) *Autonomous technology: technics-out-of-control as a theme in political thought* (Cambridge, Massachusetts: MIT Press).

[267] Hughes T (1994) Technological momentum, in *Does technology drive history? The dilemma of technological determinism*, Smith M, and Marx L (Editors) (Cambridge, Massachusetts: MIT Press).

4.16 'Technological determinism' in this sense describes a state of affairs in which it is alleged that social relations, for example, are determined by technology more than technology is determined by social relations. Such determinism may be seen as doubly potent because it operates through both the material and discursive contexts, for example in the way societies become inured to new and potentially 'dehumanising' relationships with the world through technology, that might have seemed intolerable at earlier points in time.[268] Therefore, the public interest in biotechnology is in ensuring that social forces control the progress of technology rather than being controlled by it.

Public ethics

The public good

4.17 The interests of individuals in biotechnologies within communities will not always coincide. This is inevitable because the impact of biotechnologies will not be restricted to cases in which all individuals share an interest in common (e.g. security) but will also extend to areas in which those interests conflict (e.g. prioritisation of resource use). The notion of a public interest that transcends aggregate individual interests is associated with social contract theorists. The modern thinker most associated with this approach is the American political philosopher, John Rawls. Rawls suggested that citizens presented with the challenge of designing the rules for a state but ignorant of the place that each would take up in it would agree on at least one good that is common to all, namely, justice for all.[269] Thinking through the choices involved in designing a political association, Rawls suggested that people should be able to consent to a political arrangement in which their interests must sometimes be compromised for the sake of what would become, by their consenting, 'the common good'.

4.18 This liberal democratic view of common good has tended to overshadow a different conception of the common good,[270] originating in Aristotle, which sees it as an end that is shared by members of a community.[271] The argument in favour of the attempt to identify common ends rather than the protection of individual freedoms is essentially this: if biotechnologies are potentially transformative, it is not enough simply to protect and balance freedoms, since the technologies adopted transform the scope and meaning of freedom for all.[272] Therefore it is not a matter of one or more individuals having more or less freedom vis-à-vis one or more others, but of the choice of technology transforming the scope of the freedoms available to all.[273] Furthermore, it may do so in a non-trivial – and practically irreversible – way by processes of lock-in and feedback and transformation that we have discussed.[274] So, because a biotechnology choice is potentially 'enframing' (in other words, it alters the horizon of possibilities for the collective), it is a choice that can only be exercised in relation to the collective.

4.19 The promise of significant transformations in society from biotechnologies implies that it is not possible to adopt them while insulating sections of society from the consequences of doing so

[268] See, for example, Heidegger M (1977) *The question concerning technology and other essays* (New York and London: Garland Publishing).
[269] Rawls J (1972) *A theory of justice* (Oxford: Clarendon Press).
[270] At least until comparatively recently, with the revival of virtue ethics and theory. See, for example, the work of Elizabeth Anscombe, Alasdair MacIntyre, Martha Nussbaum and Amartya Sen.
[271] The use of the term 'common good' does not imply the notion that there is a good that is common to all who have an interest, of the 'lowest common denominator' type – a solution that all can tolerate but that serves none. It is a political concept that emerges from the interrelatedness of a group of heterogeneous individuals orientated towards a particular set of conditions which they experience together (technological opportunities and the threat of climate change or economic catastrophe, for example). We note that there is some confusion surrounding the terms 'common good' and 'public good' in the literature (common good deriving from the modern, individualistic tradition and public good from the tradition of Aristotle and Aquinas).
[272] In other words, they are 'enframing'; see: Heidegger M (1977) *The question concerning technology and other essays* (New York and London: Garland Publishing).
[273] In some circumstances, as we suggest in the section on global public goods, this can be the case at the global level. See paragraph 4.8.
[274] See paragraphs 1.27 to 1.33 and 3.22 to 3.25.

(in the long run, at least) and that by adopting them, it will become progressively difficult, perhaps practically impossible, to resile from the path chosen. They therefore require us to confront questions of public good rather than the focus narrowly on the management of harms and the protection of individual liberties. This is the task of public ethics.

Public ethics

4.20 The field of bioethics is noticeably developing greater competence in questions at the public level. Bioethics, at least in the US and Europe, has often approached the evaluation of new technologies from the individualistic tradition in which it was initially rooted as an academic discipline. Within this broad tradition, there are differences between approaches that are grounded primarily in individual freedom and personal autonomy, and those that are based on positive rights. More recently, however, in the context of increasing globalisation, and of threats to collective well-being from environmental damage and pandemic disease, concepts of collective interest and collective action have moved to the fore. Some have identified the development and application of these concepts as a major re-orientation within bioethics, a 'communitarian turn',[275] which in turn offers new responses to areas addressed by traditional medical ethics. This new orientation is towards a notion of the public good rather than – and distinct from – the concern for negotiation between individual interests engaged by bioethical questions.

4.21 The implications of this reorientation are significant. They alter entirely the way in which technological development and innovation must be approached in discourse and in practice: rather than focusing on outcomes, products and impacts on individuals, the focus shifts onto broader social contexts, circumstances, implications, and alternatives. Advocacy of a particular choice is replaced by interrogation of assumptions on which the choice is founded; commitments and the pursuit of achievement leavened by caution and the concern for (opportunity) costs. Public ethics, like the provision of public goods, is a matter of collective consideration and action.

4.22 In a society that accommodates plural values, it is no longer plausible to suggest that the end of ethical reflection is a single, rational answer to the question "what is the good life?" This pluralism is compounded by the global reach of many questions about biotechnology (that, furthermore, often demand prompt and unilateral answers). But it is because of this pluralism and the 'public' nature of biotechnologies, that the task of determining the conditions of collective life has become such an urgent ethical question in the technological age. In such conditions, an ethical basis for action is not one that can be found by a single thinker reasoning in isolation but one that is to be established instead through a discursive engagement between differing perspectives. The work of public ethics is to establish the *context* of biotechnology governance. It is less concerned with following through 'impacts' than working back to assumptions.

Developing new biotechnologies as a moral mission

4.23 The reason most frequently given for developing new biotechnologies is that they promise ways to increase human welfare and well-being, that is, to avoid or alleviate harms and to secure benefits. Given that reducing harm and increasing benefit may be taken as a generally desirable aim, the case in favour of biotechnology research, development and innovation embodies a strong *prima facie* sense of moral mission. The capacity of biotechnologies to contribute benefits in health care, food and energy supply, and environmental and economic prosperity means that there are strong ethical reasons to support their development and, other things being equal, the development of as many biotechnologies as promise these benefits.

[275] See: Chadwick R (2011) The communitarian turn: myth or reality? *Cambridge Quarterly of Healthcare Ethics* **20**: 546-53. The Nuffield Council on Bioethics' own recent Report on solidarity as an emerging concept in bioethics may be seen as a contribution both to understanding and developing this thought. See: Prainsack B and Buyx A (2011) *Solidarity: reflections on an emerging concept in bioethics*, available at: http://www.nuffieldbioethics.org/solidarity-0.

4.24 According to the canonical definition of 'utility' proposed by JS Mill "actions are right in proportion as they tend to promote happiness, wrong as they tend to produce the reverse of happiness."[276] The difficulty in applying this evaluation to emerging biotechnologies is that their 'tendency' to produce one thing or the other comes up hard against a paucity of evidence, either of their production of these effects, or of relevant experiences from which such effects can be inferred reliably. In fact we know it is plausible that most prospective biotechnologies will actually not provide benefits, for the reason that they encounter hard constraints and fail during development, for example, or because they are crowded out by more dominant technologies.[277] Some technologies, we know, actually produce harms, although these may not be easily foreseen.[278]

4.25 A second consideration that tempers this *prima facie* ethical argument for biotechnology is the possible existence of opportunity costs, in the form of foregone opportunities to develop alternatives approaches. If there is a real possibility of alternatives that would be preferable (at least from some perspectives) being crowded out by contingent conditions that facilitate the development of those that *are* developed, this might result in foregoing some utility that would otherwise be available.

4.26 If we acknowledge uncertainty as an irreducible characteristic of emerging biotechnologies, the claims that any particular biotechnology will produce particular outcomes or 'impacts' must be treated with circumspection. This does not mean that the pursuit of particular outcomes is unethical; indeed, it is indispensible. The point of this scepticism is to draw attention to the error of committing prematurely to two sorts of potential frame: firstly, construing social 'challenges' as hypothecated to technological solutions (in general or particular) and therefore curtailing the exploration of other kinds of possible response; secondly, focusing the development of biotechnologies too tightly on solutions to particular challenges and therefore failing to be sensitive to the range of possible benefits they might bring, perhaps in radically different contexts.

4.27 In any case, what counts as a benefit or harm, or of whose happiness or unhappiness is relevant, may well be contested in the case of biotechnologies.[279] Such contested questions are clearly difficult to resolve, but that is what makes them the proper matter of bioethics.

Public values

4.28 In posing questions of public ethics, we wish to set out three underlying values that we believe should guide biotechnology assessment. Their point of application is the expectations and imaginaries that animate attitudes towards biotechnologies and orientate decisions relating to them. Their aim is to broaden out reflection on these orientations to take account of potential transformative effects – including effects on the structure of society – and opportunity costs. We do not claim these values are necessarily and eternally valid: they are simply those that, in relation to the emergence of biotechnologies in the present historical context, appear to us to be most important, taking into account the public interest in biotechnologies, and the broader context that prompts the 'biotechnology wager'.

[276] Mill JS (1863) *Utilitarianism* (London: Phoenix, 1993), p6.
[277] See paragraphs 1.26, 1.31 and 2.41.
[278] Such as CFCs or asbestos, as discussed in Box 1.1.
[279] As the authors of an ethical framework for stem cell research in the EU observe: "This question has proved resistant to resolution through philosophical analysis or by scientific definitions. The moral status, or degrees of protection to be accorded to the embryo is constituted linguistically, culturally, scientifically, politically and through religious and secular beliefs." Eurostem (2005) *An ethical framework for stem cell research*, available at: http://www.eirma.org/sites/www.eirma.org/files/doc/pubs/briefs/0410stemcell-ethframe.pdf/noproxy, p2.

Equity

The value of equity requires equal respect for the entitlements, interests and preferences of others, including in questions of fair and just distribution of expected benefits and costs.

4.29 This value implies a respect for freedom from discrimination but also the opportunity of groups and individuals to pursue their interests in different ways. The principle recognises the fact that different groups and individuals value different outcomes and states of being differently, and that not all equalities are fair and that not all inequalities are unfair. It provides a bulwark against the legitimate interests of individuals being set aside in the interests of the collective, or rather, it expresses the thought that it is in the interest of the collective that the interests of its *individual members* should not be set aside in this way, as the protection of such interests is important to the social enterprise. As such it implies the principle of 'just reward', which may be operationalised, for example, through upholding the rule of law (e.g. preventing theft), market conditions and the protection of intellectual property.

Solidarity

The value of solidarity requires the avoidance of social divisiveness and exploitation, and the active promotion of the welfare of those who are less advantaged.

4.30 While equity includes the thought that not all inequalities are unfair, some inequalities are manifestly *harmful* to certain groups. Poverty, hunger and sickness, for example, are not *necessarily* a matter of individual responsibility or the collective choices of groups that are affected by them. Biotechnologies may have the potential to decrease or increase social division, for example by offering advantages to those who can afford them that further widen existing social differences or, conversely, tackling problems that predominantly affect the most disadvantaged. Valuing solidarity therefore encourages us, recognising our own relative advantage and our capacity to help those who are less advantaged, to bear costs on behalf of others[280] including costs of research and providing knowledge. It also enjoins us to explore the implications of contending innovation trajectories, including those favoured by more marginal groups. Even in cases where such disadvantage is the result of a choice or judgment on the part of the disadvantaged, there is a moral case, one that highlights shared humanity and the contingency of differences between individual conditions, that disadvantaged people deserve our sympathy and assistance, rather than our censure.

Sustainability

The value of sustainability requires the avoidance of significant or irreversible depletion of exhaustible natural resources, or damage to ecosystems or the wider environment. It therefore favours the development of more sustainable alternatives to existing technologies.

4.31 The original formulation of the principle of sustainability focuses on "meeting the needs of the present without compromising the ability of future generations to meet their own needs".[281] This limits the pursuit of short term benefits where they may harm equally important long term interests or lead to relatively poorer conditions of well-being or welfare for future generations. In this sense the principle of sustainability gives the principle of equity an intergenerational aspect. It is notable, particularly in view of what we have said about the discursive basis of public ethics, that the value of 'sustainability' was first developed within social movements and outside institutional governance structures, but was subsequently institutionalised and is now accepted as an important bulwark defending the long term interests of society and of future generations against short term political, commercial or professional interests.

[280] See: Prainsack B and Buyx A (2011) *Solidarity: reflections on an emerging concept in bioethics*, available at: http://www.nuffieldbioethics.org/solidarity-0, paragraph 29ff.

[281] This is the formulation by the 'Brundtland Commission' (World Commission on Environment and Development), maintained in subsequent international policy discourse up to the present Millennium Development Goals. See: United Nations World Commission on Environment and Development (1987) *Our common future*, available at: http://www.un-documents.net/wced-ocf.htm.

4.32 Biotechnologies may, for example, address the unsustainability of current technologies by providing replacement technologies (for example, next generation biofuels for transport), or provide for future needs that cannot be met through existing means (e.g. food production). It is in this way the notion of sustainability arises as a driver for technological development.[282]

Developing new biotechnologies as a *prima facie* moral good

4.33 Insofar as the pursuit of biotechnologies is orientated towards advancing welfare in a way that is consistent with the values of equity, solidarity and sustainability, or towards promoting these values without a concomitant decrease in welfare, we believe that such initiatives constitute a *prima facie* moral good.[283] We believe that it is important to state this positive interest in the development of biotechnologies clearly as a positive ethical reason for biotechnology research and innovation. One reason for doing so is that, too often, ethical reflection can come to be seen as an impediment to research: slowing things down, holding back developments and innovations, rather than a primary source of motivation – for pushing ahead and making progress. The challenge now is how to move from here to normative conclusions in the context of practical uncertainties, ambiguities and equally uncertain and ambiguous alternatives.

Public ethics *in situ*

Normative complexity

4.34 Normative propositions express values or prescriptions. This is in contrast to descriptive propositions that represent factual states of affairs. In this Report we have been dealing with different discursive contexts including technical, social, political and economic contexts, and, of course, ethics. When asking any practical question, such as what is to be done in a given set of circumstances, there needs to be an implicit understanding of what kinds of normative consideration are relevant to determining the answer. For example, if the question is what to wear it might be social (dress conventions) or prudential ('wear a raincoat if you don't want to get wet'); if the question is about whether to tell the truth the source may be ethical ('it is wrong to tell a lie').

4.35 Although it is important to understand what kinds of normative considerations are relevant to answering practical questions, in reality most practical questions are complex and draw on different sources of normativity. There is therefore scope for ambiguity about the meaning of normative terms like 'good', 'bad', 'right', 'wrong', 'ought', 'must', etc., when applied to things like research proposals, business plans or policy options: what is 'good' or 'bad' can differ, as we saw in Chapter 3, according to whether it is seen from a technical, social or ethical perspective. For example, while enforced vaccination may be technically 'good' as a way of preventing the spread of potentially epidemic disease (it is an efficient way of achieving the objective), it may be ethically 'bad' (because it prevents individuals exercising autonomy).

4.36 When addressing complex questions of this sort it is easy to see the danger of, say, a technical perspective becoming over-dominant or of a relevant ethical perspective being ignored or suppressed. In facing complex practical questions these perspectives are commonly put together – government policy, particularly in science, relies heavily on advice from scientists

[282] For example, in October 2009, the UK's Technology Strategy Board launched an 'innovation platform' which focused on sustainable agriculture and food with the aim of increasing crop and livestock productivity whilst at the same time decreasing environmental impact. For a discussion of this platform, see: House of Commons Science and Technology Committee (2010) *Bioengineering – seventh report of session 2009-10*, available at: http://www.publications.parliament.uk/pa/cm200910/cmselect/cmsctech/220/220.pdf, paragraph 55. See also the EU's Europe 2020 growth strategy, which is based on the four priorities of smart growth, sustainable growth, inclusive growth and economic governance, available at: http://ec.europa.eu/europe2020/index_en.htm.

[283] See also the Nuffield Council's approach in its recent report on biofuels, which highlighted a moral duty to develop biofuels: Nuffield Council on Bioethics (2011) *Biofuels: ethical issues*, available at: http://www.nuffieldbioethics.org/biofuels-0, paragraph 4.46ff.

and, in business, from industry. Biotechnology – which can be seen as a science-based business or a business-enabled science –will rely on advice from both of these sources and several more besides. We have been referring to the process by which they are brought together – the encounter between different normative propositions, conducted through language and expressed in speech and writing – as a 'discourse'.

4.37 The picture becomes more complicated as a result of the potential for a number of different normative conclusions to be possible within any given discursive context. Different ways of framing a question can, as we argued in Chapter 3, lead to empirical 'facts' being construed in different ways, and the way people understand a concept depends not only on whether they are a scientist or a politician (and on which scientific theory or political party they espouse), but also on contingent facts about their individual histories, personal circumstances, education or culture. Frames, therefore, cut across disciplinary and discursive contexts, and across individuals and groups. Particular frames can become dominant in each discursive context (for example, that of the eminent professor within a research discipline or the finance director within industry).

Identifying normative partiality

4.38 The first task of a more open and reflective approach to biotechnology governance is the identification of cases in which there is a public interest and where there is a danger that deliberation is framed largely in terms of sectional interests and dominated by particular forms of normativity (for example, economic or technical forms). This may be caused or compounded by the isolation of the discourses from engagement with other perspectives. The restrictive framing of such questions and the failure to make this framing explicit is recognised as the most insidious dimension of power. Of course, the exercise of power is not in itself to be deplored; indeed, it is essential for achieving any positive social end. What makes power insidious in this sense is when the framings in accordance with which it is deployed are rendered so invisible and unaccountable that the idea of questioning them does not suggest itself, and might even appear absurd. Alternatives are deleted not by argument or by force, but by the circumscribing of imagination itself.[284] This is not to imply any malign intention on the part of those in whom power is vested. It is rather to draw attention to phenomena such as the invisible effects of socialisation and the self-reinforcing dynamics of elites that lead to the phenomena we discussed in Chapter 2, namely, dissonance between the discourse on biotechnologies, on the one hand, and the material states of affairs to which they relate, on the other.[285]

4.39 It is therefore first necessary to awaken a critical reflection on the framing of biotechnology decisions, which might be achieved in a practical and constructive way through a number of straightforward questions.[286] To open up ethical deliberation in this way may appear to run against the grain of much technology decision making, which has acquired some of its sense of importance from the urgency with which we are often told it must be approached. In technology decisions, to act slowly is often presented as a failure, to cede strategic advantage to potential competitors, to miss opportunities to allow remediable harms to persist. However, opening up these opportunities does not mean to call a halt to technology but rather that recognition is given to the need to put in place appropriate measures to recognise public interests and counteract the potential premature locking in of a particular technological trajectory. It is, as we have said above, about creating a context that frames operational decision making rather than intervening in a process of decision making ('tick box ethics') that is already framed by unexamined forces and forms of normativity.

[284] See: Lukes S (2005) *Power: a radical view*, Second Edition (London: Macmillan). Also available online at: http://www.polsci.chula.ac.th/pitch/tgcm12/ps1.pdf.

[285] See paragraph 2.30ff.

[286] The 'critical' aspect of the approach may be characterised as an 'opening up' of technology selection (for example, through confrontation with alternative framings) that reveals implicit value commitments and the underlying dynamics of power. See, for example, Stirling A (2011) From enlightenment to enablement: opening up choices for innovation, in *The innovation for development report 2009-2010*, López-Claros A (Editor) (Basingstoke: Palgrave Macmilan); Stirling A (2008) "Opening up" and "closing down": power, participation, and pluralism in the social appraisal of technology *Science, Technology & Human Values* **33**: 262-94. See also responses to the Working Party's consultation, notably that of Cesagen (ESRC Centre for Economic and Social Aspects of Genomics).

Box 4.1: Identifying closures

The following series of general questions offer ways to illuminate the framing of emerging biotechnologies. Their effect should be one of assisting greater reflection over the terms and conditions of closure.

- Are there incentives that actively consider and explore a full range of alternative research, development and innovation pathways?
- Do all those who stand to be affected enjoy a direct voice in debates over regulation and research?
- Has due attention been given to the full depth and scope of complexity, ambiguity and uncertainty?
- Is a suitably legitimate balance struck between consideration of alternative views of pros and cons?
- Has there been explicit reflection on the ways power shapes choices and associated understandings?
- Is there confidence that positive and negative impacts will, in practice, be equitably socially distributed?
- Do measures and practices exist to ensure accountability and responsibility in the face of surprise?
- Is the political nature of social choice of emerging biotechnologies subject to appropriate democratic governance?
- Has appropriate consideration been given to the benefits and barriers to adoption of the emerging biotechnology, relative to alternative technologies, both those in prospect and what is already available?

4.40 A negative response to one of these questions would indicate a potential form of closure, of a kind that might be judged to require additional justification. It would then follow that what would count as cogent justification might, in turn, be judged in accordance with one or more of the values set out in this Chapter. In other words, the recognition of this kind of closure is the first step in opening up opportunities for public ethics.

Applying public ethics: towards a public discourse ethics

4.41 When we say that biotechnology governance is 'a matter of public ethics', we do not mean that all the conditions that govern biotechnology emergence should be set by 'the public' or 'in public', or that biotechnology research and development should be restricted to the public sector. That would rather unnecessarily inhibit legitimate private and commercial activities. What we mean by public ethics is that, given that there *is* a public interest in emerging biotechnologies, and *insofar as there is* a public interest, normative propositions can be made about emerging biotechnologies that are guided by the good of the public collectively. In virtue of their public role, a corresponding duty falls on public authorities to use their powers in accordance with such normative propositions, if they (the propositions) can be publicly identified. A similar injunction would fall on individuals, groups or firms as a matter of moral responsibility.

4.42 From what has been said above, it should be clear that we regard finding the terms of an unbiased and open engagement between relevant normative positions, mediated through different interpretive frames, as being the proper subject of an 'ethics' of emerging biotechnology governance. The way in which this may be achieved is through what we will call a 'public discourse ethics'.[287] This is essentially a method for determining matters of public interest 'publicly' and in accordance with the public good. It implies that the determination of conditions shaping the emergence of biotechnologies should be 'public' in two senses: those of being *non-private* and *non-partial*.

- *Non-privacy* means that the determinations in which there is a public interest, while not necessarily taking place 'before the public' (in a public forum or broadcast), nevertheless do not exclude the possibility of public scrutiny or influence. So, for example, it should be possible

[287] This approach may appear to owe some debt to the 'discourse ethics' of the 'Frankfurt school' philosopher and sociologist, Jürgen Habermas (see Habermas J (1983) *Moral consciousness and communicative action* (Cambridge, Massachusetts: MIT Press, 2001), although it employs a more transpersonal (rather than intersubjective) concept of framing than perhaps Habermas would allow and does not share the expectation that something like an ideal speech community can be constructed around questions concerning biotechnologies.

for interested parties to know that such a determination is to be made, who is charged with making it and how they may make representations, including higher representations concerning the nature of process or the competence or conduct of those responsible. (Public determinations in this sense are contrasted with decisions made by anonymous and unaccountable powers behind closed doors.)

- *Non-partiality* means that determinations in which there is a public interest should not be made in accordance with a conditional or private good but should be orientated by promotion of the public good and therefore strive to determine the nature of the public good in relation to the determination to be made. Public determinations in this sense are contrasted with subordinating public decision making (deliberately or inadvertently) to the pursuit of private or sectional interests. So, if proponents of a given biotechnology build their arguments for why it should be supported and facilitated on claims that it will have public benefits, then consistency entails that public interests should be taken properly into account in decision making about the technology. It is not necessary that those involved should be free from all personal interest in the decision but this must be subordinated to and subsumed within the public good.[288]

Procedural virtues

4.43 We set out below a number of virtues that are intended to foster a public discourse ethics in practice, addressing the problems of privacy and partiality. We are not here primarily talking about virtues attaching to individual people involved in governance, but institutional and procedural virtues that concern the way in which policy is developed and governance conducted. Our reasons for setting out virtues in this way are twofold.

4.44 Firstly, the uncertainty and ambiguity that characterise emerging biotechnologies make the use of criteria or decision rules to guide actions difficult, since it is not possible to anticipate what kinds of actions might satisfy such rules or criteria. On the contrary, it is precisely the *frameworks* of rules, and the conditions of their application, that are in question here. Rather than concrete prescriptions, for emerging biotechnologies we must therefore look to how the business of policy making and governance is carried out, rather than its substantive content.

4.45 The second reason is that the diversity of emerging biotechnologies means that our approach must be developed at a relatively abstract level. The virtues therefore have a broad scope of application such as to enable the development of action-guiding principles in a variety of concrete contexts. We have therefore avoided setting out specific principles in favour of ways of acting that can be cultivated in a wide variety of contexts. It is also important that they are cultivated by all those engaged in biotechnology policy and governance, rather than merely followed by those in positions of authority: a public discourse ethics strives for the establishment of common ground through balanced engagement, even if operationalising it may rely on authority and power.

Openness and inclusion

The virtue of openness and inclusion is the virtue of members of society having the information and, where appropriate, access required to participate in biotechnology governance; it embodies respect for the potential plurality of views on how biotechnology choices might be framed.

4.46 The virtue of openness and inclusion reflects the fundamental public interest in biotechnologies and in their potential to affect, beneficially or detrimentally, the common conditions of life. The cultivation of this virtue is intended to offset the potential for dominance by sectional interests and to draw attention to any power structures that result in legitimate interests being excluded (for example, through control of publication media). It does not entail, of course, that members

[288] This calls to mind the Enlightenment ideal of the public use of reason (see Kant I (1784) An answer to the question: 'what is Enlightenment?', in *Kant: political writings*, Reiss H (Editor) (Cambridge: Cambridge University Press, 1991)). This, however, somewhat idealises the human spirit and places too much faith in individuals as rational seekers of truth. Instead we put our faith here in open and fairly conducted discursive engagement to confront partiality with its alternatives, in conditions that mitigate against prejudice regarding the outcome.

of the public should be involved in all biotechnology governance, nor even necessarily that all governance decisions themselves should be democratically mandated. Furthermore, even the benefits of public access to information must be balanced against the potential harms that may arise if that information is capable of being misused, for example, when there are irreconcilable threats to security.

Accountability

The virtue of accountability involves an explicit acknowledgment and acceptance of where responsibility for governance lies, how this responsibility connects with democratic lines of accountability and (therefore) how social actors might influence it or seek to have it revised.

4.47 The virtue of accountability has a variety of different meanings depending on the context, but these are united by the notion of the obligation to render an account for the exercise of power vested in an actor on behalf of others. For example political accountability, in a democratic political system, requires that members of the executive answer for their actions to the people or their elected representatives (in Parliament).

4.48 Non-political forms of accountability exist through all sorts of different social, professional and business structures. The difficulty for social participation in these is the accountability of those structures themselves, so the public interest may, for example, justify the imposition of a principle requiring constructive engagement with a broader range of perspectives in aspects of biotechnology governance that have significance for common life.[289]

Public reasoning

The virtue of public reasoning is the cultivation of clear and explicit reasoning orientated towards the discovery of common grounds rather than in the service of sectional interests, and the impartial interpretation of all relevant available evidence.

4.49 The virtue of public reasoning counteracts the habits of instrumental reasoning. When engaging in public policy or governance, it is not sufficient to rely on the assumptions and commonplaces that are customary in professional or social contexts. This is not merely a quality to be developed in individuals (although it certainly applies to individuals) but more importantly a property of discursive engagements in which matters of public interest are at stake, through challenge and argument. Reflection on reasons and reasoning is intended to address biases such as 'groupthink' and 'framing effects' to which groups and influential individuals who participate in discourses may be vulnerable.[290] For this to be the case the reasoning by which conclusions are asserted needs to be open and explicit and the interpretation of any evidence relied upon clear and open to interrogation. Symmetrically, the reason for disregarding any apparently germane evidence should be equally explicit. For example, in professional life, executives of pharmaceutical firms may wish to select from among clinical trial results evidence that supports the case for the clinical utility of the drug that they are trying to sell.[291] In a public discourse, in contrast, the full range of evidence needs to be adduced.

Candour

The virtue of candour encourages uncertainties associated with emerging biotechnologies to be represented truthfully and in good faith.

[289] For example, the research councils could be mandated to consult with social groups on questions of sustainability.
[290] See: Kahneman D (2011) *Thinking, fast and slow* (New York: Farrar, Straus and Giroux).
[291] See, for example, House of Commons Health Committee (2005) *The influence of the pharmaceutical industry (fourth report of session 2004–05) HC 42-I*, available at: http://www.parliament.the-stationery-office.co.uk/pa/cm200405/cmselect/cmhealth/42/42.pdf.

4.50 In the evidence we have considered, there was significant concern about the danger of systematic 'overstating' of the anticipated impacts and delivery timescales of biotechnology research.[292] Those who shared this concern included scientific researchers involved in the very emerging biotechnologies that they perceived as being overstated. We infer from what we have heard that, in emerging biotechnology research, a kind of systematic distortion is often encouraged, about which many researchers feel uncomfortable. On the other hand, a similar concern exists in relation to over-exaggerating the potential for harms, or over-interpreting evidence of risk. While participants may understand and accept the 'language games' in which they are embroiled, and are therefore able to discount hyperbole, these language games may spill into other discursive contexts, effectively misinforming other audiences. Furthermore, resulting over-expectations of feasibility and timescale for anticipated applications and impacts may have distorting effects on technology pathways (for example by attracting support and resources to one line of research at the expense of others).

4.51 This may be partly a consequence of expectations placed on researchers as a result of institutional structures, such as the emphasis that research councils place on the 'impact' of research.[293] Such expectations may make demands beyond the competence of researchers who are unlikely to have expertise in commercialisation, for example, or understand the timescales, processes and obstacles involved. This concern is not restricted to researchers, however: it is just as relevant to political and commercial actors, and interest groups. Public scientists often find themselves in a double bind: they need to be both *candid* (in order to be trusted), and *decisive*. However, candour is often about uncertainty and, in a context where certainty is judged to be a measure of competence, this may create a tension between candour and the appearance of competence.[294] The virtue of candour can only be inculcated by a systematic deflation of overpromising across all fields of research (so that no field of research is disadvantaged vis-à-vis any other by suddenly appearing more uncertain) and a change in the expectations of policy making, which demands clear answers and avoids engaging with radical uncertainty.

Enablement

The virtue of enablement supports wider political debate about emerging biotechnologies. It encourages appraisals of emerging biotechnologies – whether expert or broader participatory appraisals – to highlight, in a balanced way, alternative social and technological choices and their associated rationales rather than asserting single, ostensibly definitive prescriptive conclusions.

4.52 Effective appraisal of a technology option should not merely address questions such as "yes or no?", "how much?" or "how fast?". Instead, it should focus on the enabling of choice so that attention can extend beyond the anticipated benefit or harm of a single innovation, and identify other actual or possible alternatives.[295] This goes beyond the virtues of 'openness', 'accountability' and 'public reasoning', in that each of these may be equally expressed by focusing simply on particular biotechnologies. The virtue of enablement, on the other hand,

[292] Oral evidence from the fact-finding meeting on policy, regulation and governance, held by the Working Party, 8 July 2011; the PHG Foundation, responding to the Working Party's consultation: "One problem in the field of genomics is that there is a tendency towards researchers overstating the likely benefits of the research and understating the risks involved."

[293] Oral evidence from the fact-finding meeting on research and development, held by the Working Party, 6 May 2011. See also, for example: EPSRC (2012) *Delivering impact*, available at: http://www.epsrc.ac.uk/plans/implementingdeliveryplan/goals/deliveringimpact/Pages/default.aspx and BBSRC (2012) *BBSRC research grants: the guide*, available at: http://www.bbsrc.ac.uk/web/FILES/Guidelines/grants-guide.pdf.

[294] See: John S and Lewens T (2010) *The universal ethical code for scientists and the 'crisis of trust in science': report to the Science and Trust Working Group*, available at: http://interactive.bis.gov.uk/scienceandsociety/site/trust/files/2010/03/Ethical-Codes-and-Trust-16-Feb-20101.pdf, p25: "...scientific work, particularly in cutting-edge areas, is often characterised by high levels of disagreement and uncertainty. Presenting this uncertainty and disagreement to the public might be the best way in which to act sincerely. Unfortunately, it may also be the best way in which to appear incompetent." See also: Science and Trust Expert Working Group (2010) *Science and Trust Expert Group report and action plan*, available at: http://scienceandsociety.bis.gov.uk/trust/files/2010/03/Accessible-BIS-R9201-URN10-699-FAW.pdf.

[295] European Science and Technology Observatory (1999) *On science and precaution in the management of technological risk,* available at: http://ftp.jrc.es/EURdoc/eur19056en.pdf; O'Brien M (2000) *Making better environmental decisions: an alternative to risk assessment* (Cambridge, Massachusetts: MIT Press); European Environment Agency (2001) *Late lessons from early warnings: the precautionary principle 1896-2000,* available at: http://www.eea.europa.eu/publications/environmental_issue_report_2001_22; Leach M, Scoones I and Stirling A (Editors) (2010) *Dynamic sustainabilities: technology, environment, social justice* (London: Earthscan).

encourages consideration to extend to alternative options that offer credible alternative pathways to the achievement of stated social ends. In this sense, the virtue of enablement is a crucial defence against the 'instrumentalisation' of the governance of emerging biotechnologies that restricts consideration only to the means by which a given technology is developed, rather than the more fundamental 'ends' towards which this development (alongside many others) might be orientated.

Caution

The virtue of caution means that the greater the degree of exposure to uncertainty and ambiguity, the greater the responsibility deliberately to gather deeper and more extensive knowledge prior to making policy commitments.

4.53 In these terms, the virtue of caution concerns the nature and quality of the appraisal process through which alternative courses of action (and inaction) come to be examined. It contrasts with the relatively narrow and closed form of conventional regulatory risk assessment (focusing on a single proposed product, in relation to the probabilities of specific defined possibilities of harm). Instead, caution urges that, as uncertainty and ambiguity increase, correspondingly greater attention, effort and time should be devoted to:

- broadening the array of issues that are considered (e.g. indirect as well as direct effects);
- gathering a diversity of relevant knowledge on each of these (e.g. different disciplines and specialist expertise);
- engaging a plurality of different perspectives (e.g. experiences, values, interests);
- symmetrically interrogating a range of alternative options (including that of 'doing nothing');
- weighing up both the pros and the cons of each option (rather than considering just 'risks' or 'acceptability'); and
- exploring a variety of potential scenarios (to address different possible notions of pessimism or optimism) and deliberation over general qualities of different technologies that might not otherwise come to the fore (like their reversibility, flexibility, diversity and adaptability in the event of surprise).

4.54 In these terms, then, it is important to recognise that caution is not about irrational fear of novelty, nor necessarily about imposing bans, nor in any way at odds with science. It is about helping to guide the direction of innovation under uncertainty and ambiguity.

4.55 In stating this virtue of caution we are conscious of the weight of literature that has grown up around the 'precautionary principle' and the various interpretations to which that principle has been subject. Our formulation here is intended to capture what many regard as the authentic force of the precautionary principle. However, by avoiding this specific terminology we hope to avoid an engagement with what, for our purposes, would be distracting academic – or tactically misleading political – debates.

Conclusion

4.56 In this Chapter we have endorsed the claim that there is a *prima facie* moral case for developing some biotechnologies (to alleviate harms and increase welfare), but that the public interest in governance comes, in part, from biotechnology's potential to generate harms as well as benefits and, importantly, to lock in the technologies that generate these harms/benefits and crowd out alternatives. The *prima facie* case cannot therefore be further advanced owing to ambiguity and uncertainty, independently of broader reflection and concrete experience. We do not state as independent values either the pursuit of benefit or the avoidance of harm. Although they implicitly underlie our ethical approach, we recognise that the pursuit of benefit and avoidance

of harm mean different things to different people. We nevertheless identify three key values to qualify the pursuit of benefit and avoidance of harm at a public level (equity, solidarity and sustainability).

4.57 In setting out an ethical approach we wished to avoid the temptation to propose simply a supplementary set of 'decision rules' that can be applied to a set of available options to select an 'ethically preferable' option. It would not be possible to establish a single set of rules that would operate consistently for early-stage emerging biotechnologies where the applications and products are speculative, subject to high levels of unpredictability and without clear precedent. Instead, we have proposed a number of procedural virtues to which we believe the practice of discursive decision making should aspire (openness, accountability, public reasoning, candour, enablement and caution). These are intended to open up decisions to ethical reflection and provide a bulwark against undue concentrations of power within research systems, to render the exercise of power more transparent and deliberate, and so amenable to professional and democratic accountability.

4.58 The choice of ethical values and procedural virtues that we advance here is, of course, no less ambiguous or contested than any other framing, but it has two important virtues. Firstly, in terms of procedure, it aims to ensure that questions of social and ethical value and conduct are raised in public discourse and, having been raised, should be pursued alongside questions of prudential values such as economic return. Secondly, it comprises, in effect, a set of conceptual tools with which questions of value and conduct may be addressed.

4.59 In discussing the ethics of emerging biotechnologies we are aware that we are not the first or only body – and will undoubtedly not be the last – to do so, either in the particular (synthetic biology, stem cell research, stratified medicine, etc.) or the more general (emerging technology, responsible innovation, etc.). The Nuffield Council on Bioethics has itself produced a number of earlier reports on particular contemporary emerging biotechnologies, including xenotransplantation (1996), genetically modified crops (1999) and biofuels (2011).[296] In preparing our Report, we have consulted many of these sources, from a number of different independent, professional and official bodies, national and international organisations, and from different political, legal and cultural traditions, although there are no doubt more that have escaped our attention. We have profited greatly and drawn freely from these, but we do not claim in any way to have synthesised or supplanted them. We do, however, believe that the approach advanced in this Report, if applied to the governance of biotechnology, will provide a useful tool to open up and reframe decision making processes in a way that makes them more ethically robust.

[296] Copies of all Nuffield Council on Bioethics reports can be accessed via: http://www.nuffieldbioethics.org/previous-projects.

Part 2

The contexts of emerging biotechnologies

Chapter 5

Public perspectives

Chapter 5 - Public perspectives

Chapter overview

In this Chapter we consider the role of non-specialists in the shaping of emerging biotechnologies, in particular through deliberate public engagement on the part of researchers and policy makers.

We examine the aims of public engagement and distinguish normative, instrumental and substantive rationales for public engagement. We then suggest reasons why public engagement might contribute to more robust public decision making with regard to emerging biotechnologies.

We survey the modes and methods of public engagement, drawing attention to the need to tailor the method to the specific context and the fact that all methods have both advantages and limitations. Crucially, these perceived pros and cons also vary with the underlying purposes attributed to public engagement, such that designs are also always to some extent political – and themselves require open deliberation. Nevertheless they may all contribute to an ecosystem of engagement which has positive benefits.

We then set out a number of dilemmas that arise within public engagement. These include: the implications for engagement under upstream conditions of high uncertainty; the significance of – and attempt to attach a democratic value to – consensus among a small group of non-specialists; the need to be independent of policy process and yet contribute to it; the balance between informing views and eliciting them; the frequently top-down and invited nature of public engagement; and the argument that market signals provide more authentic information than limited public engagement.

Finally we address the question of why science and technology, and biotechnology especially, should require public engagement more than other areas of policy, concluding that there are institutional features of the governance system for science and technology that make it particularly appropriate.

Introduction

5.1 As we have characterised them, emerging biotechnologies are shaped by a complex variety of hard and soft conditions (from physical laws to influential personal enthusiasms). Many of these conditions are set in place as a result of the decisions or dispositions of a range of individuals, social groups or institutional bodies ('actors'). Different actors may bring to these decisions different understandings of what is at stake and what is desirable (an expert may represent a technical understanding, an industrialist an understanding of market economy, an ethicist an understanding of moral values, etc.). But even a single individual contemplating a practical decision – a politician, for example – may need to resolve different perspectives that co-exist for them as an office holder, a member of a social group, a scientist, a parent, a patient and so on. As we observed in the previous Chapter,[297] questions of practical action involve a variety of these sources of normativity and cannot be reduced to exclusively technical, social, or moral questions. Addressing all such questions therefore requires finding the appropriate conditions of engagement between these normative influences.

5.2 In this Chapter we consider methods by which decision makers engage with actors who are not professionally involved in policy and governance, as bearers of a broader range of normative perspectives. As a tool for operationalising public discourse ethics, 'public engagement', implying the engagement between those accountable for a given range of practical decisions and those who have a public interest in their outcomes, is neither necessary nor sufficient for ethically robust decision making but it may contribute both positively and, occasionally, negatively to this, depending on how it is used.

5.3 The perceived importance of public engagement undoubtedly rises where there is acknowledgment of uncertainty and ambiguity. The presence of these characteristics implies that contrasting perspectives are possible on what count as relevant frameworks for ethical decision making in the first place. How such engagements are framed is at least as important as who is involved and, indeed, whether they occur at all.

5.4 The difficulties of reaching decisions for society, formidable though they are, do not mean that no common ground is possible. It might be found more easily, however, if impossible standards

[297] See paragraph 4.34ff.

are not set at the outset. For example, we should not expect to discover a single, ideal process through which an enduring consensus can be reached on matters of public ethics. Worries and uncertainties are likely to persist, ambiguities will remain, and scepticism and dissent is not only inevitable, but healthy and productive.

5.5 An ethically robust research and innovation policy should seek to understand the reasons that underpin different and competing responses to emerging biotechnologies. This is the aim of many exercises in public engagement around different emerging biotechnologies. This Chapter will therefore consider the various ways in which such engagement may help to shape emerging biotechnologies and responses to the benefits and hazards they hold.

The Public, publics and public perspectives

5.6 In this Chapter we deal with the roles of social actors who are not recognised or involved as specialists in any of the key contexts that frame understandings of emerging biotechnologies. These include relevant interest and user groups (for instance patients, workers, consumers, or local communities), wider civil society organisations and social movements (like political parties, environmentalists, unions and faith groups), other affected businesses and agencies, as well as citizens in the most general sense. No matter how remote they are from those who exercise power within the innovation systems in question, all such social actors may hold legitimate interests in the possible outcomes and can play a role in shaping emerging biotechnologies for public good. It is typically in civil society, after all, that normative frameworks first emerge, which later come to be adopted by the institutions that shape research and innovation systems, and even by commercial firms.[298]

5.7 A term often used for the broadest level of aggregation of these non-specialists is 'the Public'. This term evokes both the agglomeration of diverse social interests and perspectives, as well as the open public arena within which they are expressed.[299] The use of the singular term 'the Public' should not be taken to imply homogeneity. Indeed, grouping together diverse perspectives in this way risks effacing the very diversities that are so crucial to understanding the frames that account for the appearance and disappearance of uncertainty, ambiguity and transformative potential in discourse on emerging biotechnologies. The use of the singular definite article also suggests that *the* Public exists in a sense that independent of the issues in question. In very real senses, however, it is often the other way around.[300] Many social scientists and public engagement practitioners therefore prefer the plural term 'publics'.[301] Recognising that these terms *are* contested, we refer to this collection of disparate interests and values as 'public perspectives'.

5.8 It is important to recognise that public perspectives may inform policy and governance of emerging biotechnologies in a variety of ways other than by deliberate attempts to engage them. Indeed, anticipations or presuppositions about the balance of public opinion may be hugely influential and energetically disputed even in the absence of an attempt to explore those

[298] One example is the value of 'sustainability' – see paragraphs 4.31 and 4.32.

[299] The importance of the public sphere, as distinct from that of political administration, originates historically in the Enlightenment, when national policies began to have significance for the wider population, in particular the literate bourgeoisie, through the growth of organised industry and trade (including international trade). As a result, information about the state's activities and an ability to influence these grew in importance, and was served by the contemporary growth of media (such as pamphlets and newspapers). See: Habermas J (1962) *The structural transformation of the public sphere: an inquiry into a category of bourgeois society* (Cambridge, Massachusetts: MIT Press, 1991; translated 1989). The 'public sphere' of the 19th Century was, of course, still exclusive of those such as the poor, women and the illiterate. Habermas regards it as one of the failures of the Enlightenment project that the public sphere subsequently declined into a sphere of minority sectional interests with a complacent majority, public information into journalism and publicity, and political participation into market capitalism.

[300] Dewey J (1927) *The public and its problems* (Athens, Ohio: Ohio University Press, 1989).

[301] See, for example, National Co-ordinating Centre on Public Engagement (2012) *Who are the public?*, available at: http://www.publicengagement.ac.uk/what/who-are-the-public.

perspectives directly through engagement.[302] Insofar as these have their roots in actual public perspectives, they may be mediated (and also selected, interpreted, parodied or resisted) through a variety of channels, including the established media that work alongside, or as alternatives, to deliberate engagement.

The role of the media and the engaged public

5.9 People require information if they are to become engaged meaningfully in discourse in the public sphere. In the first place, they need to become aware of biotechnologies and the discourse around them, then they need information that allows them to participate in this discourse. They may receive this through various public media. Some people – including some of those who are recruited into public engagement exercises – may become engaged despite little direct prior familiarity with biotechnologies.

The media and the public

5.10 In order to understand the role of the media – by which we mean the mass media and media targeted towards interested non-specialists – as enabling or constraining public discourse, we need to ask several questions: first, where those who are not already professionally engaged with biotechnologies receive their information; second, the extent to which the media influence their opinions about biotechnologies; and third, how the media itself is influenced in terms of how it selects (or deselects) and presents the information it publishes. At a more general level, understanding the effect of the media may also contribute to understanding the processes of discursive closure and lock-in discussed earlier and also to identifying opportunities to 'open up' reflection and debate in the public sphere.

5.11 It is a common premise in communication studies that the media have significant effects on public opinions.[303] Despite the stability of this premise it is surprisingly hard to find evidence of the range and relative importance of sources of information about biotechnology used by non-professionals, although it is probably safe to conclude that much of it comes via public media[304] that are increasingly modulated by online sources such as websites, forums or blogs. It is similarly difficult to find evidence that sheds clear light on the way in which, and the extent to which, mass media influence the qualitative nature of public opinions. One relevant programme of research is cultivation analysis, which studies the long term effects of exposure to media portrayals – in particular television – on people's perception of social reality. Evidence from cultivation studies in the US concludes that there is a measurable cultivation effect in relation to attitudes towards science.[305]

5.12 Given that there is a link between controversies in biotechnology and higher levels of public awareness about biotechnologies[306] it seems clear that the media are capable of focusing and amplifying public reactions, although assessing the extent to which they qualitatively influence

---

[302] For example, in relation to genetic modification, certain decisions have been taken not to pursue GM food trials (or sales) because of public opinion and direct action groups, both at the industry level and at the governmental level. See: Hickman L (2012) GM crops: protesters go back to the battlefields *The Guardian* 22 May, available at: http://www.guardian.co.uk/environment/2012/may/22/gm-crops-protesters-battlefields and Randerson J (2012) The GM debate is growing up *The Guardian* 30 May, available at: http://www.guardian.co.uk/commentisfree/2012/may/30/gm-debate-grown-up, for discussion of how public opinion influenced GM crop use in the UK and how the debate has changed since the late 1990s and early 2000s.

[303] See, for example, the observation that "The entire study of mass communication is based on the premise that the media have significant effects." McQuail D (1994) *Mass communication theory: an introduction*, Third Edition (Thousand Oaks, California: Sage) quoted in Scheufele DA (1999) Framing as a theory of media effects *Journal of Communication* **49**: 103-22.

[304] See, for example, Gerbner G (1987) Science on television: how it affects public conceptions *Issues in Science and Technology* **3**: 109-15, where it was stated that "From our ongoing research project, called Cultural Indicators, we know that most U.S. citizens encounter science and technology most often on television."

[305] "The more people watch television the less favourable they are about science." Ibid.

[306] See: Gaskell G, Stares S, Allansdottir A, *et al*. (2010) *Europeans and Biotechnology in 2010: winds of change? A report to the European Commission's Directorate-General for Research*, available at: http://ec.europa.eu/public_opinion/archives/ebs/ebs_341_winds_en.pdf and Gaskell G, Allum N, Bauer M, *et al*. (2003) *Ambivalent GM nation? Public attitudes to biotechnology in the UK, 1991-2002*, available at: http://ec.europa.eu/research/biosociety/pdf/ambivalent_gm_nation_uk.pdf.

those opinions is less straightforward. Academic research on media effects has itself adopted and rejected a number of models in its comparatively brief history. Early research was dominated by the experience of propaganda in the Second World War and was characterised by concern over the apparent power of direct media effects on public opinion. However, this model gave way to a second stage (to the late 1960s) which saw media as essentially reinforcing existing attitudes rather than actively changing them. Subsequent research (particularly in the 1970s) has examined the cognitive effects of media presentation on beliefs, understandings and memories and to the way in which public opinion and media choices influence each other as a system, or as part of a system involving other influences besides.[307] Internet-enabled social networking is doubtless now one of these influences, and one that will further confound any attempt to explain media effects in terms of simple causes, and therefore to control them.

5.13 Despite the changing tides in scholarship about the way media influence public opinion generally, comparative studies of North American and European media show a consistent correlation between the respective media cultures and public opinion in the regions in which they predominate.[308] News media are more often expected to be objective and balanced in North America but are understood to be more opinionated in Europe,[309] correlating with greater levels of public controversy over biotechnologies in Europe than in North America[310]; however, the reasons for this correlation are apparently complex (going beyond the binary relationship between the media and public and making it difficult to identify what produces the correlation).[311]

Power and the media

5.14 What seems clearer than the influence of the media over public opinion is the influence sectional interests are capable of exercising over the media. Sectional interests may exert influence by controlling what information gets published in the first place. This can effectively keep discourse on biotechnology policy, in which there is a public interest, out of the public sphere. Such cases have been described as “uncontroversies” and “nondecisions”.[312]

5.15 Research has shown that, during the last three decades of the 20th Century, framing in the US media of issues associated with biotechnology (e.g. *in vitro* fertilisation, genetic engineering, stem cells, gene therapy, and cloning) was dominated by certain powerful media outlets and sectional interests.[313] Views that diverge from the official or orthodox can be erased progressively from public discourse through a “spiral of silence” that socially marginalises those

[307] Scheufele DA and Tewksbury D (2007) Framing, agenda setting, and priming: the evolution of three media effects models *Journal of Communication* **57**: 9-20; Scheufele DA (1999) Framing as a theory of media effects *Journal of Communication* **49**: 103-22.

[308] Gaskell G, Einsiedel E, Priest S *et al.* (2001) Troubled waters: the Atlantic divide on biotechnology policy, in *Biotechnology 1996-2000: the years of controversy*, Gaskell G, and Bauer MW (Editors) (London: Science Museum).

[309] That is to say, news media in Europe are often assumed to have an overt political stance acting as a lens through which their news and editorials are presented (and understood), while in North America the expectation is more often that the media report newsworthy occurrences in as neutral a manner as possible, with the political view of the organisation only showing through in the ‘op-ed’ sections of its output. The extent to which this is actually the case is, of course, open to debate.

[310] However, Gaskell *et al*. contest that conclusions based on this may be attributable to third person effects where people are predisposed to *overestimate* the effects of media on persons other than themselves and they “question explanations which rest on widely discredited theories of strong, direct and uniform media effects on news consumers“. Ibid, p103.

[311] Gaskell G, Einsiedel E, Priest S *et al.* (2001) Troubled waters: the Atlantic divide on biotechnology policy, in *Biotechnology 1996-2000: the years of controversy*, Gaskell G, and Bauer MW (Editors) (London: Science Museum), p113.

[312] Nisbet MC and Lewenstein BV (2002) Biotechnology and the American media: the policy process and the elite press, 1970 to 1999 *Science Communication* **23**: 359-91. The examples given are the reformulation of US federal biotechnology regulation to the advantage of industry in the late 1980s and the lack of attention given to the large amount of biotechnology research with military applications funded by the US Department of Defense.

[313] Ibid.

who express dissenting opinions.[314] This is observed despite the US media's vaunted culture of objectivity.[315]

5.16 What is particularly stark in the US experience is how interests compete to control the media portrayal of the issues in ways that strategically advantage those who have a vested interest. Furthermore there is an identifiable hierarchy of influence, at the apex of which is government, followed by industry and trusted professions, followed by civil society groups that have become adept at using publicity methods arising in commercial marketing. The goal of this competition is always the eradication of ambiguity and the assertion of one view as official, or right-thinking, while delegitimising dissenting perspectives.[316] Alignments between industry, policy makers and scientists were most effective, for example, in securing public support for agricultural biotechnology as a solution to declining farm incomes, beguiling investors during the early 1980s with upbeat press releases and optimistic government reports into believing biotechnology offered a new kind of blue chip stock.[317] On the other hand, controversy surrounding biotechnologies has surfaced at rare points, when dissenting voices were able to find expression through the media (two points noted in the US were around the wider implications of recombinant DNA and human cloning[318]). Despite the divergences in journalistic culture, and the greater frequency of reporting of controversy in Europe, research has still found scientific, industrial and political elites dominant in setting the news agenda and content in the UK and Germany as in the US.[319]

5.17 The partial framing of biotechnology issues by the media need not be deliberate. It may also stem from the "shared culture" of scientists and science journalists who are often themselves scientifically trained and may see themselves as bridging the professions of science and journalism.[320] However, another perspective on this is offered by a study of the perceptions scientists and journalists have of media reporting of biotechnology.[321] The study found a dissonance between the views of the two groups: while both agreed that reporting should be sober and measured, perceptions of actual reporting differed, with scientists, unlike journalists, tending to view it as too sensationalist and focused on risks.

5.18 As we acknowledged in Chapter 2, framing is a necessary part of the process of reducing the complexity of an issue in order to communicate what is significant about it to non-specialists. This is particularly the case given the constraints, in terms of time or space, of news media.[322] In the presentation of biotechnologies in the media a number of distinct framings have been identified,[323] each of which attends to different aspects of significance.

---

[314] See: Noelle-Neumann E (1993) *The spiral of silence: public opinion – our social skin* (Chicago, Illinois: University of Chicago Press).

[315] A noted paradoxical result of the US media's culture of striving for 'balance' was the undue prominence that climate change scepticism continued to receive despite a stable and widespread consensus on this issue. See: Gaskell G, Einsiedel E, Priest S *et al.* (2001) Troubled waters: the Atlantic divide on biotechnology policy, in *Biotechnology 1996-2000: the years of controversy*, Gaskell G, and Bauer MW (Editors) (London: Science Museum), p9.

[316] Nisbet MC and Lewenstein BV (2002) Biotechnology and the American media: the policy process and the elite press, 1970 to 1999 *Science Communication* **23**: 359-91.

[317] We discuss the 1980s 'biotechnology boom' in Chapter 9. See paragraph 9.5.

[318] Bioethicists have also understood the importance of influencing the news agenda with some success: see Nisbet MC and Lewenstein BV (2002) Biotechnology and the American media: the policy process and the elite press, 1970 to 1999 *Science Communication* **23**: 359-91.

[319] Listerman T (2010) Framing of science issues in opinion-leading news: international comparison of biotechnology issue coverage *Public Understanding of Science* **19**: 5-15.

[320] Nisbet MC and Lewenstein BV (2002) Biotechnology and the American media: the policy process and the elite press, 1970 to 1999 *Science Communication* **23**: 359-91, p366.

[321] Gunter B, Kinderlerer J and Beyleveld D (1999) The media and public understanding of biotechnology: a survey of scientists and journalists *Science Communication* **20**: 373-94.

[322] Scheufele DA and Tewksbury D (2007) Framing, agenda setting, and priming: the evolution of three media effects models *Journal of Communication* **57**: 9-20, citing Gans HJ (1979) *Deciding what's news* (New York: Pantheon Books).

[323] Durant, Bauer and Gaskell, for example, develop a typology of eight framings (Durant J, Bauer MW and Gaskell G (1998) *Biotechnology in the public sphere: a European sourcebook* (London: Science Museum)) cited in Nisbet MC and Lewenstein BV (2002) Biotechnology and the American media: the policy process and the elite press, 1970 to 1999 *Science Communication* **23**: 359-91; Listerman identifies five framings (Listerman T (2010) Framing of science issues in opinion-leading news: international comparison of biotechnology issue coverage *Public Understanding of Science* **19**: 5-15); Nisbet, Brossard and Kroepsch identify 11 in relation to the media presentation of controversy relating to stem cells (Nisbet MC,

Box 5.1: A framing typology for biotechnology

- *Progress:* celebration of new development, breakthrough; direction of history; conflict between progressive/conservative-reactionary
- *Economic prospect:* economic potential; prospects for investment and profits; research and development arguments
- *Ethical:* call for ethical principles; thresholds; boundaries; distinctions between acceptable/ unacceptable risks in discussions on known risks; dilemmas. Professional ethics.
- *Pandora's box:* call for restraint in the face of the unknown risk; the opening of flood gates warning; unknown risks as anticipated threats; catastrophe warning
- *Runaway:* fatalism after the innovation; having adopted the new technology/products, a price may well have to be paid in the future; no control any more after the event
- *Nature/nurture:* environmental versus genetic determination; inheritance issues
- *Public accountability:* call for public control, participation, public involvement; regulatory mechanisms; private versus public interests
- *Globalization:* call for global perspective; national competitiveness within a global economy; opposite: splendid isolation

This typology was used in a large-scale study of biotechnology related coverage in the *New York Times* and *Newsweek* over a period of nearly two decades.[324] This was adapted from a typology used in an earlier study of print overage of biotechnology across 10 EU countries.[325]

5.19 We can conclude that media representations of biotechnology and associated issues may inform and influence (as well as reflect) public perceptions of biotechnology, although the mechanisms and effects are complex. Media presentations of biotechnologies are, however, susceptible to deliberate, strategic control as well as inadvertent cultural partiality, and sectional interests can exert a significant influence on how the media frames the issues associated with them. Industry, political and scientific elites appear to be particularly responsible for this, as well as other interest groups, including civil society groups opposed to biotechnologies (although these latter are less successful in North America than Europe). The media are nevertheless an important part of a system that can create shared understandings and enable participation in the public sphere.

Rationales for public engagement

5.20 We can see that discourse in the public sphere is subject to partial framings and the attentions of sectional interests. Can public engagement create the conditions for an encounter between these framings that might produce a public basis on which to construct and evaluate policy and governance decisions more systematically, robustly and legitimately?

5.21 Before we begin to consider the uses and limitations of different approaches to public engagement in different circumstances it is necessary to be clear about why we are interested in public engagement as a possible mode of operation of public discourse ethics. Amid the complexities of different approaches and methods of public engagement, it is easily forgotten that the term is often used, quite legitimately, to refer to activities undertaken for radically different reasons.

5.22 The political stakes around public engagement compound the difficulty of balanced discussion of these general underlying issues. For example, a range of commentaries have asserted that the 2001 UK GM Dialogue process was problematic. This might seem to imply that the design or implementation was deficient in some particular fashion. Yet the underlying reasons for many

Brossard D and Kroepsch A (2003) Framing science: the stem cell controversy in an age of press/politics *The International Journal of Press/Politics* **8**: 36-70).

[324] Nisbet MC and Lewenstein BV (2002) Biotechnology and the American media: the policy process and the elite press, 1970 to 1999 *Science Communication* **23**: 359-91.

[325] Durant J, Bauer MW and Gaskell G (1998) *Biotechnology in the public sphere: a European sourcebook* (London: Science Museum).

of these concerns were actually contradictory. Some felt the process was deficient because the outcome failed sufficiently to support a policy that was of unquestionable merit. Others were concerned about lack of uptake of engagement outcomes in actual policy making. Some questioned the representativeness of the process; others the folly of striving for representativeness. The resource and time constraints were also criticised by some as a lack of commitment to the process and an attempt to diminish its influence. Engagement exercises may in fact be unwittingly 'designed to fail' if they are circumscribed in their conception for fear of contradicting a preferred outcome.[326]

5.23 As a result of these kinds of difficulty, debates over public engagement can easily become polarised around simplistic 'pro' or 'anti' caricatures. We should therefore not try to assess the advantages and disadvantages of public engagement in general, or the merits or drawbacks of different specific methods, without being clear about the particular aims.

5.24 A useful way to think about these issues was proposed in 1989 by the US Environmental Protection Agency official, Dan Fiorino. This framework distinguishes different reasons for public engagement according to whether they are normative, instrumental or substantive, and has been adopted in a number of influential policy reports on the challenges of public engagement in relation to the governance of innovation, notably the 1996 US National Research Council report *Understanding risk*.[327]

5.25 A **normative** rationale for public engagement is that it is a self-evidently positive process, simply because it is the *right thing to do* in a democratic society. Despite the many different conceptualisations of what a democracy is, or should be, notions of political equality and popular sovereignty are generally treated as axiomatic.[328] From a normative perspective the question of whether public participation is important is turned on its head to become: 'why should we *not* involve public perspectives in societal decision making?' Evaluation of public engagement under a normative perspective will focus on various qualities of the process itself (like inclusiveness, legitimacy, representativeness, accessibility, transparency and freedom of expression) that affect the ways in which public understandings, interests and values are addressed. A crucial point is that this view focuses only on the effective practice of participatory deliberation as a process, irrespective of the outcomes.[329]

5.26 An **instrumental** rationale, on the other hand, focuses directly on outcomes. Here, the use of participatory deliberation in public engagement is seen not as an end in itself, but as a means to some pre-defined end. It is a way to *get the right answer*. Of course, the particular ends in

---

[326] One key criterion referred to in the official evaluation of the GM dialogue process was the need for public engagement to yield outcomes that are usable in policy. If 'not usable' means not supporting the policy direction favoured by the sponsors, which is therefore of no use to them, the exercise may be assessed as deficient on those grounds. For more on this topic, and instances of contenting criticisms of the 'GM dialogue' process, see: Defra (2004) *The GM public debate: lessons learned from the process*, available at: http://webarchive.nationalarchives.gov.uk/20081023141438/http://www.defra.gov.uk/environment/gm/crops/debate/pdf/gmdebate-lessons.pdf; Defra (2004) *The GM dialogue: Government response*, available at: http://webarchive.nationalarchives.gov.uk/20081023141438/http://www.defra.gov.uk/environment/gm/crops/debate/pdf/gmdialogue-response.pdf; Horlick-Jones T, Walls J, Rowe, G, Pidgeon N, Poortinga W and O'Riordan T (2004) *A deliberative future? An independent evaluation of the GM Nation? Public debate about the possible commercialisation of transgenic crops in Britain, 2003.* (Norwich: University of East Anglia); Mayer S (2003) *GM Nation? Engaging people in real debate?*, available at: http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/GMNationReport2.pdf; Wilsdon J and Willis R (2004) *See-through science: why public engagement needs to move upstream*, available at: http://www.demos.co.uk/files/Seethroughsciencefinal.pdf?1240939425; Food Ethics Council (2004) *Just knowledge? governing research on food and farming*, available at: http://www.relu.ac.uk/links/justknowledgebrief.pdf; Wynne B (2007) Public participation in science and technology: performing and obscuring a political–conceptual category mistake *East Asian Science, Technology and Society: an International Journal* **1**: 99-110.

[327] See: Stern PC and Fineberg HV (Editors) (1996) *Understanding risk: informing decisions in a democratic society* (Washington, DC: National Academy Press).

[328] Dewey J (1927) *The public and its problems* (Athens, Ohio: Ohio University Press, 1989); Habermas J (1996) *Between facts and norms: contributions to a discourse theory of law and democracy* (London: Polity Press); Warren ME (2001) Democracy and association (Princeton, New Jersey: Princeton University Press). Obviously democracy in an ancient Greek city sate is different from democracy in a modern kibbutz, not least in terms of who gets to participate.

[329] The term 'deliberation' has a specific (though no less contested) meaning in political theory. In this chapter, however, we use it in a looser manner to mean purposeful and open consideration, articulated in a public arena, of an issue of ethical or political significance.

question will differ from case to case. Sometimes participation may be seen as a means to foster greater 'trust', 'credibility' or 'legitimation' for particular institutions or technologies. At other times, instrumental objectives may highlight outcomes like 'public understanding' (according to a particular framing of an issue) or 'public acceptance' of a particular technology. Instrumentalism can, of course, just as much characterise organised participation to close off institutionally favoured choices. An instrumental perspective is apparent in an evaluative criterion that public engagement should yield results that are useful to policy makers.[330]

5.27 Finally, a **substantive** rationale for public engagement focuses on issues relating to 'public good', of the kind that concern us here. Like the instrumental view this concerns the outcomes of public engagement, rather than the process. But unlike an instrumental view, the outcomes in question are not favoured in relation to (often implicit) sectional interests. Under a substantive view, what counts as a positive outcome is determined according to explicit publicly-deliberated values. Of course, each of these values may be understood in different ways by different actors, but they nevertheless transcend sectional interests and understandings attached to particular positions, institutions or technologies. It is in transcending these interests through dialogue in this way that participants create a public frame in which social decisions may be ethically posed. In short, under a substantive view, public engagement offers a way to *make better decisions*.[331]

Purposes and values of public engagement

5.28 If a reason for carrying out public engagement is in order to make better decisions, we ought to be able to able to answer the following question: why should involving public perspectives in decisions about emerging biotechnologies lead to better decisions?

5.29 Firstly, for interdisciplinary problems of the kind we are interested in, no single individual (or community) is likely to have sufficient expertise in all the dimensions that are likely to be important. To take an example, if a decision needed to be made about whether synthetic biology could provide appropriate responses to problems of food security, not just molecular biology would have to be taken into consideration, but also questions about agronomy and economics, among other things. Indeed, the specialist knowledge implicated in such decisions typically go beyond even the entirety of organised academic disciplines, also involving – as they often do – the experience, insight and expertise of subsistence farmers, local communities, small businesses, and food consumers.

5.30 This argues for a broadening, perhaps a *radical* broadening, of the range of expertise informing decisions. But the broadening of the scope of relevant interests leads to increasing difficulty in maintaining the distinction between expert and non-expert. This is not a matter of diluting or negating disciplinary perspectives, or imagining that public engagement may somehow provide a neutral way of arbitrating among them, it is rather that the radical broadening of admitted interests turns the discursive space into a public space. It is therefore, by definition, not possible for any particular specialism to claim definitive expertise. Like other exercises in the balancing of contending positions; this is a matter for political judgment.[332]

5.31 Secondly, for questions with significant social and economic implications, the scientific experts on whom policy makers most typically rely are unlikely to possess the full range of appropriate expertise.[333] Even with respect to the social implications of a specialised and highly technical

[330] See paragraph 5.7ff.

[331] It is evident from any reflection on actual public engagement exercises that they often mix these three rationales, implicitly or explicitly. Thus they may be try to foster public trust while at the same time trying to improve the quality of decision making by engaging those who stand to be affected by the decision.

[332] See paragraphs 5.1 and 5.29. Of course, some disciplinary criteria may be agreed to be more relevant to a given decision than others and they should rightly be given more prominence – the point is that they should be agreed to be so, rather than being imposed as such.

[333] Arie Rip engagingly talks about the "folk theories" of scientists – scientists speculating about the social dimensions of their policy advice by guessing what the public thinks on the basis of their limited acquaintances, what they read in

topic, competence is multidimensional, comprising aspects of both fact and value. However, the two are not readily separable. Appreciation of scientific findings, for instance, rests on notions of proof that are dependent on background assumptions. Once again, this argues for a broadening of the range of expertise, for example to include social scientists and others who can reflect upon science as a *social practice*. One example is the way in which scientific conventions operate concerning significance and the balance to strike between avoidance of errors of Type I (wrongly concluding a false hypothesis is true) and Type II (wrongly concluding a true hypothesis is false).[334] In a research context, this may involve simply trading off the speed of development of knowledge against confidence in the robustness of that knowledge. However, when science moves into policy domains, a broader range of potential consequences begin to hinge on such judgments.[335] Instead of trading off 'robust but slow' against 'unreliable but fast' developments of knowledge, the importance of vulnerability to Type II error under these circumstances involves the balance of interests of those benefitting from the rapid knowledge gains against the interests of those who stand to be harmed. This becomes rather important where the issue involves judgments between different courses that each involve significant uncertainties, for example the need to develop a vaccine rapidly in response to a possible pandemic or the possible deployment of a weaponised pathogen.[336]

Modes and methods of public engagement

5.32 These arguments support a form of public engagement that is aimed at framing decisions of policy and governance relating to emerging biotechnologies in a way that is orientated by a notion of public good. However, the way in which this is carried out in practice can achieve this outcome with variable degrees of success. Some experiences may even be counterproductive, as some evaluations suggest,[337] insofar as their operational failures may lead not to a public discourse on policy and governance, but instead to retrenchment on all sides. Before any deliberate substantive engagement around a particular issue takes place, there therefore needs to be a prior accord about the aims and the methods of the engagement, and also about how it will be evaluated. A different way of framing this is to recognise that the engagement itself needs to be orientated towards the public good and constructed so as to be able to deliver this within the constraints of the context (for example, given the range of participants, the nature of the knowledge they bring and their interests).

5.33 Even within shared perspectives there is often a lack of consensus about what is effective public engagement in particular circumstances. In deploying the catch-all term public engagement it is therefore possible to fail to acknowledge the diversity of practical approaches and the objectives these activities seek to achieve. In order to keep this diversity in mind it will be helpful to describe briefly the primary dimensions of variation between different approaches.[338]

5.34 Perhaps the most obvious distinction that can be made among public engagement activities is in relation to the direction and nature of communication between researchers and members of the public. In what might be termed conventional science communication activities, such as

---

the newspapers and the conventional wisdom of their class. Rip A (2006) Folk theories of nanotechnologists *Science as Culture* **15**: 349-65.

[334] For more information on the concept of Type I and Type II errors, see: Stanford Encyclopedia of Philosophy (11 August 2011) *Risk*, available at: http://plato.stanford.edu/entries/risk.

[335] The lessons of experiences like those with tobacco, asbestos, lead, benzene, mercury, PCBs, dioxins, acid rain, CFCs and ionising radiation – to name only a few – show that early emphasis on avoidance of Type I errors (wrongly presuming harm) can lead to what, in retrospect, are seen as serious forms of Type II error (wrongly presuming safety). See: European Environment Agency (2001) *Late lessons from early warnings: the precautionary principle 1896-2000*, available at: http://www.eea.europa.eu/publications/environmental_issue_report_2001_22.

[336] See paragraph 3.9, Box 3.1 and paragraph 8.23.

[337] Sheufele DA and Ross JE (2011) *Modern citizenship or policy dead end? Evaluating the need for public participation in science policy making, and why public meetings may not be the answer*, available at: http://shorensteincenter.org/wp-content/uploads/2012/03/r34_scheufele.pdf.

[338] There are several studies in the literature that attempt to map out a typology of public engagement practices. See, for example, Rowe G and Frewer LJ (2005) A typology of public engagement mechanisms *Science, Technology & Human Values* **30**: 251-90. For a further discussion, see: Chilvers J (2010) *Sustainable participation? Mapping out and reflecting on the field of public dialogue on science and technology*, available at: http://www.sciencewise-erc.org.uk/cms/assets/Uploads/Strategic-Research-documents/Sustainable-Participation-report-03-10.pdf.

information campaigns, exhibitions, open-labs, social surveys, or forms of opinion research, communication can be characterised essentially as flowing in a single direction, from scientists to the public, or vice versa. These activities are important and may provide resources and stimulus for a public that is more engaged with questions on biotechnology policy and governance.

5.35 These one-way communications can be distinguished from activities that seek to achieve genuinely two-way dialogue and deliberation between the participants, of a kind that may inform decision making.[339] For an activity to constitute public engagement in this second sense, it should entail more than the presentation of 'facts' about science and technology, or the transmission of existing opinions or preferences held by some specific element of the public at a particular point in time. Rather, it should involve an exchange of views between researchers,[340] publics and other social actors, with the potential for each to inform the other's understanding of the issues at hand. This is not to imply that activities of the first kind are intrinsically negative, but rather that they constitute an *entirely different* set of procedures with different aims and objectives.

5.36 Within the broad range of activities that constitute public engagement in the second, deliberative sense, distinctions can be drawn according to the extent to which their purpose is to arrive at a consensus or recommendation for action. Some approaches, such as citizen's juries or consensus conferences specify coming to a collective decision as an explicit objective, while others, such as deliberative mapping aim primarily to make apparent the diversity of relevant perspectives.[341] The distinction is important because although consensus may be a desirable result of public engagement from a policy maker's perspective, setting this as an objective (or even as an evaluation criterion) may result in convergence to a 'lowest common denominator' position, or domination by narrow or sectional majorities.[342] Even for policy makers who think they want this, the volatile nature of engineered consensus can, in any case, make it a hazardous political commodity.

5.37 Approaches to public engagement also differ in the ways in which they define the population of interest and assemble participants. While many impose some control over the mixture of characteristics among participants, this is generally implemented through quotas that are intended to match a particular selected group of participants to the wider population of interest.[343] For instance, participants might be recruited so as to include specified numbers from groups defined by age, sex, ethnic group, and socio-economic status. Few approaches attempt to use random sampling strategies for reasons of both cost and practicality: not only would the use of random samples generally require a substantial financial outlay to recruit and involve, the useful approximation of a random sample to composition of the population from which it is drawn only begins to hold in samples that are arguably too large to enable effective deliberation.[344]

---

[339] Rowe G and Frewer LJ (2005) A typology of public engagement mechanisms *Science, Technology & Human Values* **30**: 251-90.

[340] In a dialogue model, the public may be able to call on 'experts' to provide specialist information in relation to particular disciplines. In this situation researchers' roles may involve facilitation, enabling participants to gather the information that they – the participants – determine they need in order to address the issues around which they have convened.

[341] Burgess J, Stirling A, Clark J *et al.* (2007) Deliberative mapping: a novel analytic-deliberative methodology to support contested science-policy decisions *Public Understanding of Science* **16**: 299-322.

[342] For this point, see generally: Stirling A (2008) "Opening up" and "closing down": power, participation, and pluralism in the social appraisal of technology *Science, Technology & Human Values* **33**: 262-94.

[343] Ordinarily, this would be done according to known or hypothesised population parameters, in accordance with a methodology chosen as appropriately according to the aims of the exercise, implying yet another level of framing to attend to; see paragraphs 5.50 to 5.51.

[344] A notable exception is the 'deliberative polling' methodology of James Fishkin and colleagues, although this approach is subject to high levels of differential non-response and other methodological weaknesses. For a discussion of deliberative polling methodology, see: Fishkin JS (1996) The televised deliberative poll: an experiment in democracy *The Annals of the American Academy of Political and Social Science* **546**: 132-40; for a discussion of methodological weaknesses, see: Merkle DM (1996) The polls - review: the national issues convention deliberative poll *Public Opinion Quarterly* **60**: 588-619.

Dilemmas of public engagement

5.38 From our discussion we can see how including public engagement in the development of policy and governance for emerging biotechnologies raises a set of overlapping and interacting dilemmas. Many of these can be traced back to ambiguity about the underlying aims. They give rise to questions about the appropriate approach to public engagement but also more fundamental questions about the influence of public engagement in aligning biotechnology policy with the public good. If the ways in which people are selected, invited, incentivised and directed to inform and participate in biotechnology decision making have a significant effect on subsequent technological trajectories, it must be important to be both transparent and critical about how such procedures are chosen and implemented.

5.39 We therefore conclude that the selection of procedures for public engagement should involve consideration of the likely consequences of favoured approaches relative to alternatives. There is therefore no single 'best' method of public engagement, and the choice of approaches will always involve dilemmas. If the approaches used are poorly aligned with underlying objectives, the result may be poorer, rather than better, quality outcomes.[345] However, it is also important to recognise that the identification of dilemmas and difficulties in the practical implementation of public engagement should not be taken as a rejection of the underlying rationale, whether that is normative, instrumental or substantive.

'Upstream' engagement

5.40 If engagement is seen as a means to explore claims about the balance of negative and positive consequences of particular innovation trajectories at an early stage,[346] then the kind of dilemma (the Collingridge dilemma) that we discuss in Chapter 1 arises.[347] In other words, how can decisions that strongly determine the future be made in conditions of uncertainty, where so much relevant information is lacking? In particular, what weight can be placed on the opinions of non-specialists, for whom even speculative possibilities are remote?

5.41 So-called upstream engagement that takes place when the concrete implications of research are distant and unclear may therefore focus less on the speculative implications of research and instead on the rationales for allocating resources to different social priorities, priorities to which different biotechnologies (or alternative measures) might offer a possible response. In this case, the challenges for upstream engagement become less to do with confronting substantive uncertainties in knowledge and more to do with determining the appropriate scope of the different values and interests to be included.[348]

5.42 The difficulty here is about how to make these contrasting aims and interests more visible and accountable, when the interests of those involved in particular research and innovation systems may want to narrow rather than open up the scope of alternatives. There is also the practical difficulty of identifying and, if appropriate, including potentially affected parties in the deliberative process. When the social and economic consequences of decision-making are supra-national, as is often the case in the context of emerging biotechnology, the challenge to make deliberative participation inclusive is formidable. For example, national engagement activities might yield preferences such as to invest in a certain technology to increase gross domestic product because this is deemed to be in the national interest, while a very different outcome might prevail were the activity to include potentially affected parties from the developing world.

---

[345] Dietz T and Stern PC (Editors) (2008) *Public participation in environmental assessment and decision making* (Washington, DC: National Academies Press).

[346] 'Upstream' unhelpfully evokes a sequential innovation system, which is not necessarily the case with biotechnologies, although it may be more typical of the highly managed development of new products, for example in drug development.

[347] See paragraphs 1.27 to 1.29 and Box 1.2.

[348] Wynne B (2007) Public participation in science and technology: performing and obscuring a political–conceptual category mistake *East Asian Science, Technology and Society: an International Journal* **1**: 99-110.

The imperatives of deliberation and decisiveness

5.43 Public engagement can offer a means to form consensus around concrete justifications for particular decisions. Consensus conferences and citizens' juries have aims of this sort. The strength and legitimacy of any such consensus or verdict must depend, however, on the extent to which the process can be shown to conform to democratic and deliberative principles. This, in turn, foregrounds questions about representativeness, for example: on what grounds can a small, possibly self-selected group, no matter what quality of deliberation it may achieve, be claimed to represent (or to be representative of) wider society?

5.44 If, conversely, public engagement is seen as a way of 'opening up' broader appreciation of the pros and cons of possible innovation pathways seen under different perspectives, then the representativeness difficulty is diminished. Seen with this aim in mind, the purpose is not (instrumentally) to justify a single settled verdict but, instead, to inform wider (substantive) policy debates. Rather than bringing such debates to a close it opens them up further by introducing ways in which different social values and interests may support alternative innovation trajectories.[349]

5.45 The dilemma, then, is that by opening up broader perspectives and values rather than reaching substantive consensus, public engagement denies decision makers the instrumentally useful justification for particular decisions. At the same time, it reveals the extent to which established political processes need to secure legitimacy for what will likely remain quite controversial decisions.

5.46 As it would be improper to shift the burden of decision-making from properly authorised and accountable decision makers to other groups such as advisors or consultees, **expert deliberation and public engagement exercises should report their conclusions not in the form of simple prescriptive findings but as properly qualified 'plural and conditional' advice**. A wide range of policy options may thereby still be ruled out as being inferior under any reasonable perspective. But in this case, these options can be seen to be ruled out for well-examined reasons rather than as a matter of expediency in order to arrive at a definitive conclusion. This is particularly appropriate where adjudication between alternative rationales involves inherently political matters concerning the prioritisation of contending interests or values. It is through encouraging more explicit, rigorous and accountable wider political debate that plural and conditional policy advice might help to enable more democratic social choice among and between emerging biotechnologies and their alternatives.

The imperatives of freedom of deliberation and policy relevance

5.47 A third kind of dilemma concerns another feature of the relationship between public engagement and decision making procedures around emerging biotechnologies. This is the expectation, which is prominent in many evaluation exercises, that public engagement will generate outcomes that are relevant or usable in policy making.

5.48 Seen under an instrumental perspective, where public engagement is regarded as a means to help construct crucial qualities of legitimacy, credibility and trust (even acceptance) for particular decisions, this is an essential feature for engagement to have any practical value. Such practical value is, furthermore, the justification for the often considerable allocations of time and resources involved, and without it public engagement can seem a distracting and expensive irrelevance.

5.49 The dilemma is that 'usefulness' or 'relevance' must be construed in terms of the degree to which engagement furthers a pre-determined aim; however, to frame engagement in this way

[349] Stirling A (2008) "Opening up" and "closing down": power, participation, and pluralism in the social appraisal of technology *Science, Technology & Human Values* **33**: 262-94.

prevents it from being a public (in the sense of non-partial) engagement. It is a consequence of our argument in Chapter 4 that the criteria of relevance should therefore not be narrowed to the extent that outcomes of public engagement are relevant only if they answer policy makers' questions, but instead broadened to value the extent to which they address questions of public good.[350]

Representativeness

5.50 A frequently made objection to public engagement on the deliberative model is that the few participants who *are* involved cannot stand in for the many who are not, but who may have an equal or greater interest in the outcome. Striving for representativeness is, in many cases, inspired by the attempt to escape from partiality, enacting the virtue of equity that we identified in Chapter 4.[351] As we noted above, however, given the uncertainties and the ambiguities of emerging biotechnologies (where engagement is itself a process of exploring these features), it may be impossible to identify at the end of the process, let alone at the beginning, the scope of relevant interests and therefore what would constitute a representative group. There may, in fact, be so many dimensions of interest, and these interests may cut across individuals,[352] that the attempt to produce a balanced representative sample leads to indefinite or unmanageable expansion. Conversely, given the range of other interests and concerns that any individual member of society may have, there must be a limit to their willingness and capacity to engage with all questions that potentially affect even themselves and their families.

5.51 This does not mean that engagement with few, perhaps unrepresentative, perhaps self-selecting individuals has no positive value from the point of view of public ethics, as part of the ecosystem of engagement. In the case of nanotechnology, for example, a few thousand members of the UK public have been involved in deliberative processes.[353] Why, it is asked, should such a comparatively small number be afforded particular attention compared to the 60 million or so who have not been reached? An important perspective on this is that in these events, between 50 and 100 scientists or policy makers have been directly involved in public dialogue, which is quite a significant fraction of the major professional actors involved, many of whom, as a result, will perhaps think differently about the value of different perspectives than they might otherwise have done. This is, potentially, a positive end in itself. However, it is clear that it also leaves open the possibility of scientists and policy-makers merely *appearing* to have taken public perspectives into account; if practice remains unaffected by interaction with the public, the cloak of legitimacy lent by the engagement process may be considered a worse outcome than had no public engagement taken place at all.

Informing and eliciting

5.52 The role of the public in science governance and decision making has moved on considerably from the days in which it was dominated by the 'knowledge deficit model', in which the purpose was seen as being to inform a largely ignorant and sceptical public about the 'facts' of science and technology.[354] Nonetheless, questions remain about the ability of non-specialists to acquire a sufficient grasp of complex areas of science to enable them to make meaningful and well-founded contributions to technology choice.[355] This applies equally to the ways in which different people conceptualise probability, risk and the appraisal of conflicting evidence as it does to any particular field of technical knowledge.

---

[350] See paragraph 4.49.
[351] See paragraph 4.29.
[352] As we noted in paragraphs 3.28 4.37 and 5.1, this makes their own positions ambiguous, i.e. where one individual 'represents' more than one perspective or set of interests which each must reconcile individually.
[353] See: Gavelin K, Wilson R and Doubleday R (2007) *Democratic technologies? The final report of the Nanotechnology Engagement Group (NEG)*, available at: http://www.involve.org.uk/wp-content/uploads/2011/03/Democratic-Technologies.pdf.
[354] Irwin A and Wynne B (2004) Introduction, in *Misunderstanding science? The public reconstruction of science and technology*, Irwin A, and Wynne B (Editors) (Cambridge: Cambridge University Press).
[355] Collins H and Evans R (2007) *Rethinking expertise* (Chicago, Illinois: University of Chicago Press).

5.53 The dilemma of technical competence is entwined with the issue of representativeness, insofar as some members of the public will find the technical aspects of science easier to grasp than others. It is possible for the procedures of public engagement to address absences of technical competence, for example, by involving expert informants, although such approaches have built-in limitations. There is, for example, only so much that can be achieved within time and resource constraints, and the reliance on technical expertise raises further questions about how it is selected. On the other hand, the inevitably differing competencies that participants bring to engagement activities makes it possible that the influence of existing socio-economic inequalities may be exacerbated rather than ameliorated.

5.54 The notion that public engagement should be used as a way of securing public consent for decisions made by experts is regarded with disdain by most advocates of public engagement, even though it still exists in scientific and policy discourse.[356] Nevertheless, the ideal separation between the processes of eliciting public perspectives and of conditioning them is not always possible to sustain in practice. Scientists who have sincerely and strongly held views about the desirability of a particular course of action, which they will seek to reinforce with scientific arguments, will often, in good faith, seek to persuade others to accept their points of view.[357] That is not to say that we would never support the right – and indeed the desirability – of scientists taking overtly political positions, so long as they are represented and understood as such. The problem is not with the scientists and, for the same reason, not with the lack of specialist technical competence among the lay majority, but with framing the debate in a way that privileges scientific argument where the decision is more than a technical one, and where the technical judgment and moral judgment of scientists become confused.

‘Top-down’ and ‘bottom-up’ engagement

5.55 We can distinguish between public engagement that is instigated through formal institutional channels where members of the public are invited (or recruited) to participate, and engagement that occurs in spontaneous, uninvited ways, instigated through interest groups, voluntary organisations or members of the public.[358] Whatever direction from which the initiative comes, what categorises these initiatives as engagement is the attempt, as we have noted at paragraph 5.30, to construct a public space within which to represent the issues. Nevertheless, depending on the issue and context, the origin of the initiative may have a bearing on how effectively this proceeds and the commitment that different parties have to it.

5.56 Top-down approaches are potentially problematic in that those initiating the engagement often have vested interests and instrumental reasons for doing so. On the other hand, bottom-up engagement is by nature spontaneous and responsive rather than anticipatory.

5.57 The difficulty is that, by the time a technology becomes an appropriate subject for a possible policy decision – the point at which broader engagement usually takes place – it has already emerged to a significant degree and the issues are already invested with values and expectations. An important response to this, as we have suggested in Chapter 4, is to do with cultivating an environment in which engagement is not exceptional but enabled, in which there are healthily diverse ecosystems of engagement.

[356] See, for example, Leask J, Braunack-Mayer A and Kerridge I (2011) Consent and public engagement in an era of expanded childhood immunisation *Journal of Paediatrics and Child Health* **47**: 603-7.

[357] For a discussion of scientists engaging in ‘issues advocacy’, whereby eliding scientific arguments and political positions ‘stealth issues advocates’ attempt to attach the authority of the former to the latter, see: Pielke RA (2007) *The honest broker: making sense of science in policy and politics* (Cambridge: Cambridge University Press).

[358] Wynne B (2007) Public participation in science and technology: performing and obscuring a political–conceptual category mistake *East Asian Science, Technology and Society: an International Journal* **1**: 99-110.

Governance by visible and invisible hands

5.58 If it is accepted that social and political decisions about biotechnologies should not be reserved to a private cadre of experts but should be opened up to public influence, a powerful objection to the whole notion of public engagement in technology decisions becomes that the job of selecting the most desirable innovations can be left to the free market, as the most effective means of aggregating the preferences of many different actors.[359]

5.59 A general problem with this is that any specific real-world market is fundamentally shaped and structured by its social context. Contingent power relations, distributions of resources, cultural sensibilities, institutional structures and incumbent interests – as well as socially-conditioned preferences – may well yield contrasting (but equally market based) technological preferences. In a complex, dynamic and path-dependent world, the contingent ways in which these factors have evolved historically may not present the best basis for prospective long term social choices. Conversely, as we have noted at paragraph 3.25, potentially transformative technology choices present opportunities to change these very conditions in the future. In this sense, then, markets present many of the same kinds of contingencies and challenges as a form of aggregation as does finding an ideal mode of public engagement. Although not irrelevant, markets present no more definitive a means to resolve questions of social choice, than do carefully-designed deliberative procedures. In short, neither is definitive or unconditional, but one may have a potentially important balancing effect on the other.

5.60 More specifically, although notions of preference may be useful to address the relatively straightforward process of choosing between pre-defined alternatives, governance of emerging biotechnologies is as much about the forming of alternatives as choosing between them. Furthermore, given the manifest changeability of social preferences, important questions concern where these come from and how they are conditioned. The market offers a very poor way to appreciate the multidimensional values and understandings that constitute the formation of preference and the basis of the choices made.

Biotechnological exceptionalism or the need for public engagement?

5.61 In the previous Chapter we referred to the general argument that where public money is spent on biotechnology research and development, the public should have a direct say in how it is spent.[360] One possible response to this is that anyone who asserts this view must explain *why* this spending should be any different from the many other places in which the Government spends money without direct public input, governed by the overall framework of representative democracy. Of course, such a response ignores increasingly prominent arguments concerning the general imperative towards greater public deliberation across all areas of policy making. The more opaque and technocratic the field of policy, and the more neglected in prevailing political discourse, one might say, the more force this argument has. Nevertheless, the question raises some important issues for a report of the present kind.

5.62 A more specific argument for effective public engagement in the field of biotechnology follows on from the commonly asserted claim that research should be carried out in pursuit of "widely shared societal goals".[361] To the extent that notions of public good are, implicitly or explicitly, important in debates over emerging biotechnology, the relevance of public deliberation is as clear here as elsewhere. Indeed, similar pressures for greater public engagement are arguably often as evident in other areas of public life as they are in biotechnology, especially where

[359] This assertion is associated with free-market economist and philosopher Friedrich Hayek (Hayek FA (1944) *The road to serfdom* (Chicago, Illinois: University of Chicago Press, 2007)). Such an approach has been strongly and relevantly criticised, most recently by the political philosopher Michael Sandel (see: Sandel M (2012) *What money can't buy: the moral limits of markets* (London: Allen Lane)).

[360] See paragraph 4.9.

[361] Jones R (2011) Some questions for British research policy, on *Soft Machines* [internet blog] 22 July, available at: http://www.softmachines.org/wordpress/?p=1075.

questions are raised about responsiveness or accountability (e.g. criminal justice, health care and local government).

5.63 However, in the case of biotechnologies, how the societal goals are identified and prioritised is especially salient since it is increasingly the case in the UK[362] that science and technology are steered by freestanding agencies that are deliberately set apart from government, such as the research councils, established by Royal Charters and operating under a particular understanding of the Haldane principle.[363] Institutionally, these bodies are set up to be more remote from the normal routes of parliamentary accountability than many other agencies and activities of government. The policy of such bodies (as we will discuss in Chapters 6 and 7) is nevertheless already much more strongly influenced by scientific experts and by industry voices than by the political process, so these arguably rather sectional points of view may need to be balanced by countervailing voices drawn from a wider section of society. In this sense their discursive space contrasts with public discourse, being both private and partial (according to our definition of these concepts in Chapter 4).[364]

5.64 A final, very important issue surrounds the distinctive ways in which questions of science and technology tend to be discussed in Parliament and other policy arenas. With regard to science in policy around emerging biotechnologies, the repeated emphasis remains on 'sound science'.[365] Attention typically fails to differentiate the ways in which policy can never, and should never, be solely based on science. Science of itself, in practice, rarely determines only a single possible interpretation or action. With regard to policy for science there is a similarly simplistic and unhelpful tendency to frame debates around 'pro- and anti-' dichotomies in relation to technology or innovation in general. This means that policy debates typically fail to consider the potentiality of social choice among alternative emerging biotechnology trajectories, let alone engaging with the practical details.

5.65 It is telling to compare this ubiquitous 'pro' and 'anti' language that is found in relation to technologies with the absence of what would be the comparable 'pro' and 'anti' language in areas like welfare, education or foreign policy. This same lack of differentiation is indicated by another issue we explore:[366] the lack of discrimination (despite the abundance of data) in the statistical information that is collected about research and development such as would make possible a clear public understanding of the choices that are actually being made, let alone the alternatives that might be chosen. In other words, public engagement is especially relevant in the field of emerging biotechnology, because it is precisely in this area that the normal democratic political process is most at risk of being undermined by deference to partial technical discourses and 'science based' policy that may obscure the realities of social choice between alternative scientific and technological pathways.

---

[362] See paragraph 7.10.

[363] See paragraph 7.50ff.

[364] See the Chapter 4 overview and paragraph 4.42.

[365] See, for example, House of Commons Hansard (17 November 2000) *c1209*, available at: http://www.publications.parliament.uk/pa/cm199900/cmhansrd/vo001117/debtext/01117-10.htm; House of Commons Hansard (5 December 2011) *Draft Renewable Transport Fuel Obligations (Amendment) Order 2011*, available at: http://www.publications.parliament.uk/pa/cm/cmtoday/cmstand/output/deleg/dg01111205-01.htm.

[366] See Chapter 7, below. This issue was the subject of a recommendation from a recent House of Lords Select Committee. See: House of Lords Science and Technology Committee (2010) *Setting priorities for publicly funded research – volume I: report*, available at: http://www.publications.parliament.uk/pa/ld200910/ldselect/ldsctech/104/104i.pdf, paragraph 67. See also evidence given by Professor Andrew Stirling in House of Lords Science and Technology Committee (2010) *Setting priorities for publicly funded research – volume II: evidence*, available at: http://www.publications.parliament.uk/pa/ld200910/ldselect/ldsctech/104/104ii.pdf, pp283-88. The Government's response to this recommendation, while noting problems in consistency in reporting, mainly highlights the relative abundance of data in this area, rather than acknowledging the difficulty of making practical use of those data for the important ends identified (e.g. to understand rationales behind resource allocation, departmental accountability and maintenance of national capacity). For the Government response, see Department of Business, Innovation and Skills (2010) *Government response to the House of Lords Science & Technology Select Committee report "Setting priorities for publicly funded research"*, available at: http://www.bis.gov.uk/assets/biscore/science/docs/g/10-1090-government-response-priorities-publicly-funded-research, p2.

Conclusion

5.66 In this Chapter we have considered issues related to the use of organised public engagement initiatives to inform biotechnology policy and governance. We found that the term 'the public' does not refer to a stable, homogeneous and definable group, but is characterised by distinction from those with recognised expertise or authority relevant to decisions about biotechnology policy and governance. Our earlier conclusion (Chapter 4) that emerging biotechnologies are a matter for public ethics,[367] and that public ethics is constituted by a discursive practice, orientated by the notion of public good, effaces the distinction between expert and public. 'Public perspectives' in the sense in which we have discussed them, are those of a range of social actors, all of whom may contribute to framing biotechnology choice in terms of public good. Public engagement activities therefore, in principle, provide an operational methodology for framing biotechnology policy and governance in terms of public ethics.

5.67 However, we observe that the terms on which engagement exercises are undertaken and the way in which they are incorporated as part of the processes of policy development and governance may result in their effectiveness being limited or their outcomes narrowly evaluated. We conclude that there is therefore no 'royal road' to effective engagement. Careful and critical attention must therefore be given to the alignment of the method with the underlying rationale for engagement, and the aims and expectations of engagement should be understood in advance.

5.68 We observe that the utilisation of public engagement (i.e. within in a policy or governance process) gives rise to a number of dilemmas. In no case, however, can public engagement substitute the responsibility of policy makers. We therefore conclude that the outcomes of public engagement, just like expert technical advice, should be reported in a properly contextualised and conditional way rather than as simple prescriptive advice. We conclude by extending our argument in Chapter 4 concerning the distinctive public interest in biotechnologies in a way that accounts for the special relevance of public discourse to biotechnologies. Cultivating the institutional and procedural virtues identified in Chapter 4 to develop a culture or ecosystem of engagement helps to overcome the dilemmas identified in this Chapter, with public engagement forming the context – rather than being inserted into the process – of biotechnology policy and governance.

[367] See paragraph 4.42.

Chapter 6

Research

Chapter 6 - Research

Chapter overview

In this Chapter we examine the role played by researchers in shaping the emergence of biotechnologies. We examine the influences *of* researchers on biotechnology trajectories and the influences *on* researchers that govern how their influence is brought to bear. We consider two extreme views (that researchers themselves determine the direction of their research and that researchers are merely instruments in society's attempts to achieve goals through science and technology) and ask how the changing relationship between science and society may rebalance the position of researchers between these two extremes. We also discuss the way in which this balance is struck in the UK's current arrangements for funding academic research through the research councils, and how industry visions influence the direction of publicly funded research through road-mapping exercises.

We also consider the influence on researchers of powerful imaginaries encapsulated in 'grand challenges' and argue that in framing these the broadest range of views should be involved in accordance with the principles we set out in Chapter 4, to avoid an over-emphasis on technological solutions to problems with substantial social dimensions. We then consider the effect on research of the need to demonstrate 'impact' to potential funders and conclude that this can encourage a tendency to 'overpromise' in relation to the benefits of emerging biotechnology in a way that is not supported by the science.

Finally, we discuss the role of researchers as public figures, communicating research to a wider audience and informing public decision making and the responsibilities that this entails, including consideration of how others, such as DIYbio practitioners and social scientists might enrich the practices of professional research.

Introduction

6.1 This Chapter focuses on the role of researchers in steering the development of emerging biotechnologies. Researchers do not form a homogenous group but are subject to different motivations, pressures and influences, including the kind of institution in which they work and the sources of their funding. There are perceived tensions between the 'basic research' mission of researchers in academic laboratories and the applied purposes of research carried out in more commercial environments, but simple distinctions between basic and applied research are inadequate to account for the diversity of motivations and external pressures to which researchers are subject.[368]

6.2 We also acknowledge the different roles of researchers both as influencers and as subject to influences coming directly from funders, indirectly from the wider socio-political environment, and from the emerging tendencies of the scientific enterprise as a whole. We recognise a paradox in the lack of agency of individual researchers despite their centrality in the research enterprise.

6.3 The questions that guide this Chapter are: what decisions determine the direction of research in emerging biotechnologies? How does the framing of these decisions about research priorities and trajectories get closed down? How can decisions be opened up to social and ethical values? And how can we steer the research system to maximise the contribution of research on emerging biotechnologies to the public good?

Where is research on emerging biotechnologies done?

6.4 It is extremely difficult to identify where research on emerging biotechnologies is carried out, due to the paucity of data available or its ambiguity. Some information can be gleaned from papers published in journals, from research grants awarded, and from reported information about economic activity surrounding research. However, as is perhaps to be expected in any emerging field, the categorisations are not sufficiently precise and consistent, and not used sufficiently precisely or consistently, to allow meaningful comparison or aggregation.[369]

[368] Calvert J (2006) What's special about basic research? *Science, Technology & Human Values* **31**: 199-220.
[369] The limitations are documented in research commissioned for this project from Dr Michael Hopkins and available via the Council's website. See: www.nuffieldbiothics.org/emerging-biotechnologies-evidence-reviews.

6.5 At an international level the Organisation for Economic Co-operation and Development (OECD) periodically collects statistics according to a two-part definition of biotechnologies it has developed. However, these statistics suffer from an acknowledged variability and incompleteness of responses across countries, as well as differences in methods used.[370] At the UK level, although some research councils and other agencies, such as the Medical Research Council (MRC), and the Technology Strategy Board (TSB), do make information available on grants awarded[371] there is little available analysis on aggregated levels of funding by area or technology focus.[372] For these reasons it is only possible to provide a broad-brush characterisation of institutions and groups that carry out research on emerging biotechnologies. Such institutions and groups include:

- Universities.
- Government/research council institutes, some key examples of which are:
  - Roslin Institute (Biotechnology and Biological Sciences Research Council (BBSRC) and University of Edinburgh: biosciences for livestock applications);
  - John Innes Centre (BBSRC: biosciences for crop science);
  - MRC Laboratory of Molecular Biology (MRC and University of Cambridge: disease research);
  - Francis Crick Institute (MRC, Cancer Research UK, The Wellcome Trust, University College London, Imperial College London and King's College London: interdisciplinary medical research); and
  - Wellcome Trust Sanger Institute (The Wellcome Trust, MRC: genome research).
- Large firms (such as big pharmaceutical firms).
- Small firms (typically start-ups and spin-outs).[373]

6.6 Outside such professionally constituted and recognised settings, there is also is a shifting and indefinite penumbra of research in non-institutional settings such as, for example, the 'Do-It-Yourself Biology' (DIYbio) movement.[374] Although it is difficult to ascertain the real extent and significance of such research, it is important to recognise that not all of those who may be classified as 'researchers' are operating in universities, institutes or firms.

Who funds research on emerging biotechnologies?

Research councils

6.7 It is similarly difficult to determine who funds research into emerging biotechnologies. Very few specific policies regarding 'emerging technologies' (biological or otherwise) can be found in published documents available from the UK research councils, but when they are mentioned,

[370] For OECD data collections, see: http://www.oecd.org/statisticsdata/0,3381,en_2649_34537_1_119656_1_1_1,00.html; for discussion, see: Hopkins M (2012) *Emerging biotechnologies: can we find out who funds R&D and what they support?*, available at: www.nuffieldbiothics.org/emerging-biotechnologies-evidence-reviews.

[371] These data go back to 2000 and 2004 respectively; for MRC, see: http://www.mrc.ac.uk/ResearchPortfolio/SearchPortfolio/search.htm?AdvSearch=1; for TSB, see: http://www.technologyprogramme.org.uk/site/publicRpts/default.cfm?subcat=publicRpt1. These allow searching only by a limited number of factors.

[372] See: Hopkins M (2012) *Emerging biotechnologies: can we find out who funds R&D and what they support?*, available at: www.nuffieldbiothics.org/emerging-biotechnologies-evidence-reviews.

[373] A 'spin-out', also known as a 'spin off', is either a subsidiary of a 'parent' organisation or an entirely new, independent organisation that has split-off from its parent. This may happen for a number of reasons. In this context, it is often the case that a small, independent spin-out firm is formed by splitting off from a larger, parent, academic organisation (such as a university) for the purpose of profitable commercialisation of a technology developed originally in an academic setting.

[374] Bennet G, Gilman N, Stavrianakis A and Rabinow P (2009) From synthetic biology to biohacking: are we prepared? *Nature Biotechnology* **27**: 1109-11.

their multidisciplinary nature is emphasised.[375] For example, the MRC maintains that "Working across disciplines is key to achieving the best results with new and emerging technologies".[376] As we note in Chapter 7 these documents also tend to stress the anticipated economic value of emerging technologies and the issue of exploiting that value.[377] For example, the BBSRC notes that it is "active in identifying emerging technologies where industry can derive real benefit from ideas emerging from the science base".[378] (The idea that emerging technologies lend themselves to commercialisation is arguably linked to their transformative potential, discussed in Chapter 3;[379] we discuss this assumption further in Chapter 9.)

6.8 The interdisciplinary nature of emerging biotechnologies and the uncertainty of their applications may mean that it is often hard to see who is in control of the funding; indeed coordinated control may be lacking. For researchers, this can mean that their projects fall in the gaps between different research councils; more broadly, persistent ambiguities of this kind may limit the potential for achieving social objectives.

Technology Strategy Board

6.9 The TSB, in partnership with the research councils, funds Innovation and Knowledge Centres in areas of technology that they define as emerging. These are very much orientated towards industrial exploitation. They are described as "centres of excellence with five years' funding to accelerate and promote business exploitation of an emerging research and technology field. Their key feature is a shared space and entrepreneurial environment, in which researchers, potential customers and skilled professionals from both academia and business can work side by side to scope applications, business models and routes to market."[380]

Direct funding from Government departments

6.10 Although a large proportion of UK Government funding for research is channelled through agencies such as research councils and TSB, the Government does provide some direct funding for 'emerging technologies', for example through the Ministry of Defence (MoD). Funding is provided for specific 'areas of interest',[381] although the MoD does note that these areas "will not necessarily receive direct MoD funding. In the UK, the research councils and the TSB support extensive civilian research programmes on Emerging Technologies".[382] In the US, significant funding is made available through the Defense Advanced Research Projects Agency for a very wide variety of technological initiatives.[383]

European Union

6.11 The European Union provides science and technology funding in a number of ways, perhaps the most significant of them being the Framework Programmes system: large, long-term projects with budgets running into the tens of billions of euros.[384] During the previous

[375] We extracted key references to emerging biotechnologies from a range of publications available for download from the BBSRC, MRC and Engineering and Physical Sciences Research Council, as well as carrying out keyword searches of their websites.
[376] MRC (2012) *Strategic aim four – research environment*, available at: http://www.mrc.ac.uk/About/Strategy/StrategicPlan2009-2014/StrategicAim4/Researchenvironment/index.htm.
[377] See paragraphs 7.10 to 7.17.
[378] BBSRC (2008) *Delivering excellence with impact: BBSRC delivery plan 2008-2011*, available at: http://www.bbsrc.ac.uk/web/FILES/Publications/bbsrc_delivery_plan.pdf, at p37.
[379] See paragraphs 3.22 to 3.25.
[380] TSB (2012) *Emerging technologies and industries*, available at: http://www.innovateuk.org/ourstrategy/our-focus-areas/emerging-technologies-and-industries.ashx.
[381] These are: advanced electronic and optical materials; advanced materials; autonomy; bio-inspired technologies; communications; data and information technologies; emerging quantum technologies; energy and power; future computing; high power technologies; human focused technology; medical advances from biological science; micro and nano technologies; micro electronics; system(s) integration. Ministry of Defence (2012) *Emerging technologies*, available at: http://www.science.mod.uk/strategy/dtplan/technologies_default.aspx
[382] Ibid.
[383] See, generally, http://www.darpa.mil/default.aspx.
[384] A detailed breakdown of the funding streams provided by the current Framework Programme can be found here: http://cordis.europa.eu/fp7/budget_en.html.

Framework Program (FP6) there were a number of initiatives relevant to emerging technologies: 'New and Emerging Science and Technologies' (NEST)[385] and 'Future Emerging Technologies' (FET).[386] FP6 ended in 2006; NEST programmes are no longer independently active under FP7, having been "partially incorporated into the thematic priorities of the Co-operation programme rather than operating as a separate cross-thematic activity",[387] as part of the activities of the European Research Council. FET remains active under FP7[388] and will continue, along with the activities of the European Research Council, under the category of 'Excellent Science' during the next Framework Programme ('Horizon 2020').[389]

6.12 Funding for FET has increased consistently since FP5: ~€290m during FP5, ~€325m during FP6 and a predicted ~€840m by the end of FP7. The proposed funding under the Horizon 2020 programme is €3.505 billion.[390] The FET programme now incorporates a large amount of funding for two 'flagship' projects, which are "large-scale, science-driven, research initiatives that aim to achieve a visionary goal" on a scale similar to that of the Human Genome Project. Although FET comes under the Directorate General for Communications Networks, Content and Technology, multidisciplinary pilot projects for this funding involve biotechnology elements through convergence between information and communications technology (ICT) and biology or biomedicine.[391] One of these is the 'IT Future of Medicine' pilot, which aims to realise personalised medicine through the creation of *in silico* virtual models of living patients to aid diagnosis and prescribing.[392] Another is the Human Brain Project which promises similar insights into the human brain, both to advance neuroscience and neuromedicine, and to advance computer science though emulating the brain's computational capabilities.[393]

Commercial firms

6.13 Research into emerging biotechnologies is also funded by a variety of large, small and medium-sized firms, although in many cases, with the exception of dedicated biotechnology firms, it is difficult to disentangle the extent of biotechnology research funding from other research activities. Finance may also be provided, for example, in the case of biotechnology spin-outs, by angel investors[394] and venture capitalists. We return to this sector and its role in shaping emerging biotechnologies in Chapter 9.

---

[385] See, for example, European Commission (2006) *What is NEST? Opening the frontiers of tomorrow's research*, available at: http://cordis.europa.eu/nest/whatis.htm; European Commission (2006) *New and emerging science and technologies (NEST): Specific activities covering wider field of research under the Integrating and Strengthening the European Research area (2002-2006)*, available at: http://cordis.europa.eu/search/index.cfm?fuseaction=prog.document&PG_RCN=5702828; and European Commission (2006) *Calls for proposals*, available at: http://cordis.europa.eu/fp6/dc/index.cfm?fuseaction=UserSite.NestCallsPage.

[386] Described as "an incubator and pathfinder for new ideas and themes for long-term research in the area of information and communication technologies (ICT)... [going] beyond the conventional boundaries of ICT and ventures into uncharted areas, often inspired by, and in close collaboration with, other scientific disciplines, since radical breakthroughs in ICT increasingly rely on fresh synergies, cross-pollination and convergence with different scientific disciplines (e.g. biology, chemistry, nanoscience, neuro- and cognitive science, ethology, social science, economics) and with the arts and humanities." Guy K (2011) *Workshop on future and emerging technologies*, available at: http://cordis.europa.eu/fp7/ict/programme/docs/fp7-fet-02_en.pdf, p1. See also: European Commission (2009) *Future and Emerging Technologies (FET) 2002-2006*, available at: http://cordis.europa.eu/ist/fet/home.html.

[387] See: Guy K (2011) *Workshop on future and emerging technologies*, available at: http://cordis.europa.eu/fp7/ict/programme/docs/fp7-fet-02_en.pdf, p2.

[388] European Commission (2012) *ICT - Future and emerging technologies*, available at: http://cordis.europa.eu/fp7/ict/programme/fet_en.html.

[389] Personal communication, European Commission, 25 May 2012.

[390] European Commission (2011) *Proposal for a regulation of the European Parliament and of the Council establishing Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)*, available at: http://ec.europa.eu/research/horizon2020/pdf/proposals/com(2011)_809_final.pdf, p85.

[391] For FET flagships, see: European Commission (2012) *Welcome to the FET flagship initiatives*, available at: http://cordis.europa.eu/fp7/ict/programme/fet/flagship/home_en.html.

[392] See: http://www.itfom.eu.

[393] See: http://www.humanbrainproject.eu/vision.html.

[394] Angel investors are wealthy individuals who provide capital to new businesses from their own resources, in return for certain financial rewards. They sometimes operate collectively with other such investors.

Charities and philanthropy

6.14 Emerging biotechnologies are increasingly being funded and shaped by a variety of non-governmental, and non-commercial, organisations. In some cases these have resources available that match or exceed the resources of many governments or major multinational firms. Such organisations introduce a variety of different perspectives to shape the direction of research that come neither from the scientific community nor from industry. These perspectives range from those of very wealthy individuals such as Bill Gates,[395] through to patient groups and the very wide donor bases that underlie many biomedical research charities and disease-specific non-governmental organizations. Charities and philanthropic organisations can be highly focused on the objectives of particular populations or social groups. They have a large degree of independence and are not subject to the same obligations and accountabilities as public funders, such as research councils. Examples include:

- Wellcome Trust (~£640 million on charitable activities, which includes research and public engagement);[396]
- Bill and Melinda Gates Foundation (agricultural biotechnology with a focus on Africa and the developing world, e.g. C4 rice project,[397] anti-malarial drugs using synthetic biology[398]); and
- Other medical charities (e.g. Action on Hearing Loss for stem cell treatments for deafness[399] and auditory brainstem implants[400]).

What determines the directions of research in emerging biotechnologies?

6.15 It is clear that research in emerging biotechnologies would make no progress without researchers, so the position of researchers in the process by which the biotechnologies emerge is central. However, it is less clear whether researchers, collectively, have a dominant role in dictating the directions of research or whether, in contrast, it is the effect of various external influences on researchers that is more important. In reality, it is likely that there will be a complex set of feedbacks between the influence *of* researchers and the influences *on* researchers. These issues can be highlighted by considering two contrasting positions:

- Science-led research: the scientific community collectively decides which are the most interesting directions for emerging biotechnologies, and funders, guided by peer review, support the highest quality research. Industry subsequently picks promising leads to develop further, or research is spun-out into new firms.
- Goal-directed research: funders, whether research councils, Government, charities or industry, decide on priorities for emerging biotechnologies, perhaps with reference to national or global challenges such as food security or the ageing population, or with reference to perceived commercial opportunities. Researchers then adjust their approaches to take advantage of funding opportunities that this offers.

[395] The Bill and Melinda Gates Foundation has had a major impact on health research but has been criticised by some for diverting staff and resources from more basic needs and increasing dependency. See, for example, Piller C and Smith D (2007) Unintended victims of Gates Foundation generosity *Los Angeles Times* 16 December, available at: http://www.latimes.com/news/nationworld/nation/la-na-gates16dec16,0,3743924.story.
[396] See paragraph 7.18 for more detail.
[397] See: International Rice Research Institute (2012) *All about C4 rice*, available at: c4rice.irri.org.
[398] See paragraph 2.21.
[399] Action on Hearing Loss (12 September 2012) *Human stem cells restore hearing*, available at: http://www.actiononhearingloss.org.uk/news-and-events/all-regions/press-releases/human-stem-cells-restore-hearing.aspx.
[400] Action on Hearing Loss (2012) *Improving medical devices*, available at: http://www.actiononhearingloss.org.uk/your-hearing/biomedical-research/projects-and-research/researchers-and-phd-students/researchers/improving-medical-devices/jinsheng-zhang.aspx.

6.16 Clearly neither of these positions wholly reflects what happens in reality. The first position does not provide a complete account of research as the directions scientists take are strongly determined by research for which funding is available to them. The freedom of action of an individual scientist varies: elite university-based researchers with long-term personal funding may have substantial amounts of freedom, although this is dependent on the continuation of outputs that are able to be published by major journals, while industry-based researchers may have little or no individual agency. Although both kinds of researcher will work subject to shared visions of the kind discussed in Chapter 2 (see paragraphs 2.29 to 2.38), most researchers fall somewhere on a continuum between the two extremes.

6.17 Goal-directed research also clearly has limitations. For example, researchers themselves, individually or collectively, must clearly have a role in shaping the priorities of those who fund them, and identifying the scientifically viable technologies. As we discussed in Chapters 3 and 4,[401] this influence may also be modulated by normative frames other than the technical frames generated within a scientific discipline. How strong the influence of researchers is, compared to other influences – such as the interests of industry, the priorities of government, the views of publics expressed directly and indirectly or the effects of more widely-conditioned social imaginations about the future – or how strong it should be, is an issue that it would benefit from explicit debate.

6.18 Both researchers and funders may also be influenced by unintended consequences of prevailing institutions, structures or practices. For example, the way intellectual property tends to drive research may lead to bias towards research directions that produce readily appropriable patentable outputs (namely devices or formulations) rather than research that focuses on new social processes or public knowledge.[402]

6.19 Researchers are also subject to other transnational trends and tensions in science:

- The entry of new disciplinary perspectives into existing fields can lead to new ideas about what constitutes good knowledge or valuable research. For example, with the movement of physicists and engineers into biology we see the aspiration to make biology more quantifiable and predictable.[403] Such an interdisciplinary approach is often a necessity in emerging biotechnologies because many analytical techniques rely heavily on computer science, modelling and quantitative skills.

- In many areas of emerging biotechnology there is a movement from observation to construction and from understanding to producing. This can be seen in synthetic biology where the field has grown considerably through the involvement of those interested in design and engineering possibilities. A shift towards producing devices rather than testing theories may also reflect both the drive to produce protectable intellectual property and the evolution of what high status journals regard as having the widest impact.

- In recent years, reductive approaches to bioscience such as genetics and structural biology have been superseded by more 'integrative' perspectives, such as systems biology (which studies the interactions of many individual biological components, and draws heavily on mathematical modelling). Such shifts reflect general changing attitudes to reductionism and holism.

6.20 It is also important to recognise the influence of technological development on science. What is possible in the life sciences is clearly affected by the introduction of new technologies. Sometimes these enabling technologies are consciously developed in response to the

[401] See paragraphs 3.28ff and 4.33ff, above.
[402] For a discussion of the affect of patenting on emerging biotechnologies, see Chapter 9 below.
[403] Keller EF (2005) The century beyond the gene *Journal of Biosciences* **30**: 3-10; Calvert J and Fujimura JH (2011) Calculating life? Duelling discourses in interdisciplinary systems biology *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* **42**: 155-63.

perceived needs of life sciences researchers but at other times they are developed in other contexts (usually ICT). Having been developed, their commercial availability and improvements to their ease of use allows new techniques to spread rapidly to different laboratories and research settings. Examples of this interpenetration and diffusion of techniques within different research areas include cheaper DNA sequencing and synthesis, large scale databases, robotics and microfluidics to increase the rate at which experiments can be done, and computing power to analyse results.

6.21 Because of these multiple and multi-directional influences, from some perspectives it can seem as if the direction of research in emerging biotechnologies is more an emergent property of the research system than a matter for higher level political (and democratic) control. This gives an ironic twist to our focus on 'emerging' biotechnologies in this Report. While this might be the case it does not mean, of course, that the emerging trajectories do not have socially and ethically important dimensions or that they are not conditioned by a variety of normative forces, including prevailing social and ethical dispositions.

Influences *on* researchers

6.22 The most obvious external influence on the direction of research in emerging biotechnologies is the pressure from funders of that research. When funding derives from commerce and industry, researchers will expect there to be close links between the commercial imperatives of the funding organisation and the direction of the research they are undertaking. For research carried out by start-ups and spin-outs, additional pressure is applied to researchers in situations where venture capitalists are keen to see a healthy return on their investments in relatively short timescales. Funding from charitable and philanthropic sources may also be expected to be closely targeted at meeting the goals of donors though in this case, support for 'basic science' may coexist as an explicit aim along with more focused efforts to alleviate particular conditions such as famine and disease, often through specific strategies.

Public funding

6.23 There is a balance to be struck by government funding agencies[404] when allocating resources between managed projects in support of strategic goals of the funding agency and projects that follow the priorities of individual scientists.[405] Decisions about how this balance should be struck can be contentious. In understanding the way research councils strike this balance and set their priorities, the relative importance of the following factors needs to be considered:

- the priorities of individual scientists as they emerge and are aggregated as the sum of many individual grant proposals;
- the views of elite scientists as they directly inform strategic discussions;
- the views of industrialists and financiers as they inform strategic discussions;
- direct steer from Government; and
- the influence of wider society.

6.24 The way in which research council priorities are set and operationalised is clearly important to researchers working on emerging biotechnologies. A key step for the research councils is the negotiation of their budget in the run up to the Government's four-yearly comprehensive spending review. This process begins with each research council preparing a bid document, outlining how they would use funding at various indicative levels. These documents draw on

[404] In the UK, the research councils.
[405] 'Investigator-driven research' or 'responsive mode'.

strategic plans that the research councils have drawn up with input from their advisory panels[406] and respond to societal challenges as understood by the Government. Although each research council aims to maximise the overall size of the science budget that the Treasury sets, they also want to maximise their own share of that budget in comparison to other research councils.

6.25 The research councils collaborate more closely in the choice of cross-council programmes on themes such as: 'global uncertainties' (e.g. energy, food security and proliferation of chemical, biological, radiological, nuclear and explosive weapons and technologies);[407] 'living with environmental change';[408] and 'lifelong health and wellbeing'.[409] These themes are agreed by chief executives of each research council with the expectation that each theme should be sponsored by a Government department.

6.26 Once the budget settlement is agreed, research councils then respond with more detailed delivery plans that set out, in more detail, how they will fulfil the promises made in their bid documents. Strategy and policy in the research councils are drafted by their staff; they are influenced by, and given final approval by, the governing body ('the Council') and informed by the advice of various strategic advisory panels.

Roadmaps and industry visions

6.27 Representatives of industry steer the research directions of scientists directly employed by their firms but also influence the direction of publicly-funded research through their role in providing formal advice regarding policy formation to Government and research councils. A collective view, from a business perspective, of the likely direction in which technology may unfold, and how that might be steered to the advantage both of individual businesses and wider business sectors, will influence the science funding environment and may inform the way individual scientists frame their own research proposals. (We consider the level of this influence further in Chapter 7).[410]

6.28 Firms carry out analyses of the business implications of new technologies that are relevant to the requirements of their own businesses. In some cases firms will regard these analyses as commercially confidential in the hope that the early adoption of new technology will lead to competitive advantage. Very often, however, firms may find it advantageous to act collectively to promote particular public visions of technological futures.[411] This may be motivated partly by the aim of improving public relations and partly by a desire to influence public regulatory policy. Trade associations, either national or supranational,[412] offer one vehicle for exerting such influence collectively. The trend to 'open innovation',[413] whereby firms deliberately share information with their potential competitors and customers to accelerate innovation and develop

[406] The most recent strategic plans for the BBSRC, MRC and EPSRC can be found at the following locations: http://www.bbsrc.ac.uk/web/FILES/Publications/strategic_plan_2010-2015.pdf; http://www.mrc.ac.uk/Newspublications/Publications/Strategicplan/index.htm; and http://www.epsrc.ac.uk/SiteCollectionDocuments/Publications/corporate/EPSRC_strategic_plan_2010.pdf.

[407] See: EPSRC (2012) *Global uncertainties*, available at: http://www.epsrc.ac.uk/ourportfolio/themes/globaluncertainties/Pages/default.aspx.

[408] See: RCUK (2012) *Living with environmental change (LWEC)*, available at: http://www.rcuk.ac.uk/research/xrcprogrammes/Pages/lwec.aspx.

[409] See: MRC (2012) *About LLHW*, available at: http://www.mrc.ac.uk/Ourresearch/ResearchInitiatives/LLHW/about/index.htm.

[410] See paragraph 7.44ff.

[411] This could be illustrated by almost any industry with a unified (or semi-unified) lobbying approach. Lobbying by the pharmaceutical sector, for example, might promote a collective view of medicine as a primarily biomedical enterprise. The biofuels lobby might argue for a particular understanding of climate change and energy security.

[412] For example, the UK BioIndustry Association (http://www.bioindustry.org), Biotechnology Industry Organisation (http://www.bio.org), EuropaBio (http://www.europabio.org) and Association of the British Pharmaceutical Industry (http://www.abpi.org.uk).

[413] "Open innovation is the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation, respectively. [This paradigm] assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as they look to advance their technology." Chesbrough H, Vanhaverbeke W and West J (2005) Open innovation: a new paradigm for understanding industrial innovation, in *Open innovation: researching a new paradigm*, Chesbrough H, Vanhaverbeke W, and West J (Editors) (Oxford: Oxford University Press), p1.

anticipatory markets, may provide an increasing motivation for firms to be open about their own technological priorities. Clearly, firms will wish to steer national research policy to the advantage of individual businesses or of wider business sectors, and this tendency may be embraced by governments in the pursuit of economic growth.

6.29 'Roadmapping' exercises, where the requirements for goal-orientated technology development are identified and planned, are often used to articulate and promote collective visions for technology development. These are also influenced or consolidated by related processes such as the UK Government's Foresight[414] programmes and the European Technology Platforms (relevant examples include biofuels, highlighting synthetic biology, plants for the future, and nanomedicine).[415] The approach we set out in Chapter 4 suggests that the identities of those involved in developing these visions – and the extent to which these processes tend to open up or close down discussions of future technological trajectories – are important issues, since it is often the case that only a narrow range of industrial, academic and policy participants are involved in informing the development of roadmaps.[416] In the context of emerging biotechnologies, roadmapping exercises can be potentially problematic, because there is a danger that they could prematurely push research in one direction, towards a single destination, rather than fostering a symmetrical appreciation of a diversity of possible pathways that might be explored, through the creation of what we described above as an anticipatory paradigm.[417]

6.30 Arguably, much of the power of the idea of a technology roadmap originates from one rather successful example, namely the International Technology Roadmap for Semiconductors (ITRS). This has been effective in orchestrating the actions of many independent actors to maintain the continual, exponential growth of technological capability associated with 'Moore's law'.[418] Thus, having a technology roadmap conveys the impression of purpose and inevitability in the way that a new technology is expected to unfold, and perhaps also seeks to associate the new technology with people's experience of rapid change in computer technology. It is therefore worth reflecting on whether there are particular conditions in the semiconductor industry which make the ITRS particularly powerful, and whether there is any analogy between these conditions and those that might prevail in emerging biotechnologies, particularly considering that the relative controllability of parameters in ICTs is much higher than in complex biological processes.

6.31 The ITRS is based on very well-specified future outcomes attached to definite dates in the future. This allows equipment manufacturers to design and plan the new plant that will be needed to manufacture components to the specifications in the roadmap, it prompts semiconductor firms to design new materials, identifies the research and development challenges that need to be overcome, and, not least, allows firms to identify and develop markets for the new products that will be made possible by the technological advances.

6.32 It is unlikely that emerging biotechnologies such as synthetic biology are anywhere near being able to carry out roadmapping of this sort, given the uncertainty about the reliability of the foundational technology, what it might be used for, and what the barriers are likely to be. Roadmapping-like approaches can be used for technologies at an earlier, more formative stage, but it is important that they are in a form that is appropriate to the maturity of the innovation system. For emerging technologies this may involve, for example, providing a broad framing vision of the path forward rather than setting out precise long-term technical targets.[419]

---

[414] See: http://www.bis.gov.uk/foresight.
[415] See: European Commission (2011) *European Technology Platforms*, available at: http://cordis.europa.eu/technology-platforms.
[416] See, for example, McDowall W (2012) Technology roadmaps for transition management: the case of hydrogen energy *Technological Forecasting & Social Change* **79**: 530-42.
[417] See paragraph 3.25, above.
[418] See: http://www.itrs.net; 'Moore's law', first proposed in 1965, refers to the observation that the number of transistors able to be fitted on to an integrated circuit will grow constantly at an exponential rate, approximately doubling every two years.
[419] McDowall W (2012) Technology roadmaps for transition management: the case of hydrogen energy *Technological Forecasting & Social Change* **79**: 530-42.

6.33 At the beginning of 2012, the UK Government established an initiative to produce a synthetic biology roadmap.[420] The roadmap exhibits a forceful linear narrative, supported by suggestive evidence (such as the rate of fall in the cost of gene sequencing), and presents a catalogue of new biotechnology products as virtual *faits accomplis*, despite the admission that "Synthetic biology is still at an early stage of development and relatively unproven".[421] The purpose of the roadmap is, of course, to identify the conditions that will produce this linearity (namely the funding, infrastructure, regulatory conditions, public and political support required) and it duly contains a number of recommendations to this end including building networks and capacity, investing in transfer to industry, and improving leadership and coordination.

6.34 It is very likely that the roadmap's recommendations will contribute, marginally or substantially, to the reinforcement of synthetic biology as a field of practice with its own identity. However, it would probably be a mistake to imagine that the conditions recommended to reinforce the productivity of the field are sufficient to deliver the products described in the report. Similarly, it may also be a mistake to imagine that whatever products are delivered will have required those conditions in order to be delivered. Nevertheless, the anticipatory paradigm is likely (and is indeed designed) to exert a measure of control on the emerging trajectory of synthetic biology research (and on alternative technological and social trajectories). The framing of the animating vision therefore deserves broad interrogation.

6.35 The clear focus of the roadmap is "economic growth and job creation",[422] although to its credit, it also addresses issues of responsible research and innovation, and emphases the importance of involving diverse social groups in the development of synthetic biology.[423] It is also notable that the proposed synthetic biology Leadership Council will incorporate a broader range of stakeholders than is normally the case,[424] and will meet at least once a year in public.[425] This is a development to be welcomed, although it remains to be seen whether the mechanisms designed to promote responsible innovation, such as the cross-domain collaborations and the broad background of the Leadership Council, are capable of addressing questions of public ethics and their associated ambiguities.[426] These include questions such as: are the social objectives the *right* social objectives? Why should we think that synthetic biology is a desirable (or even acceptable) way of fulfilling the social objectives identified? What should 'desirable' mean in this context (for example: 'most effective', 'safest', 'cheapest'[427]) and according to whose standard? What understanding of uncertainties should apply to the prospects of synthetic biology leading to the outcomes in terms of which its desirability is framed? (We return to this in the next Chapter.) More importantly, it is unclear (since this is not contemplated) whether these mechanisms would be able to locate the will or mobilise the power to halt research and innovation trajectories within synthetic biology if it appeared appropriate to do so.

[420] See: Willetts D (2012) *Our hi-tech future*, available at: http://www.bis.gov.uk/news/speeches/david-willetts-policy-exchange-britain-best-place-science-2012.

[421] UK Synthetic Biology Roadmap Coordination Group (2012) *A synthetic biology roadmap for the UK*, available at: http://www.innovateuk.org/_assets/tsb_syntheticbiologyroadmap.pdf, p4.

[422] Ibid. In fact, the first sentence encountered in the document is "The excellence of the UK research community provides an opportunity for future economic growth." It continues: "Deriving significant benefits also relies on the ability of business to develop products and services and on the expectation of a sizeable global market. The Technology Strategy Board highlighted synthetic biology as an emerging technology meeting all these key criteria and offering particularly strong growth potential in the UK." Ibid.

[423] Ibid, p21.

[424] Social scientists, non-governmental organisations and other stakeholders are listed as potential members of the Leadership Council in the roadmap report. Ibid, p32.

[425] Ibid. pp32-3.

[426] Ibid, p32.

[427] The Roadmap states that a condition of the broad public acceptability of innovation in synthetic biotechnology will be that it is "demonstrably directed towards ...solutions to compelling problems that are more effective, safer and/or cheaper than existing (or alternative) solutions." (Ibid, p19.)

Societal challenges and 'salvational narratives'

6.36 Over the last decade we have seen the emergence of the idea that research on emerging biotechnologies is needed to address societal challenges,[428] up to and including the notion that they are essential to avoid a global disaster, as can be found in the 'perfect storm' narrative of Sir John Beddington, the UK Government's Chief Scientific Advisor.[429] Such attitudes are embedded in the notion of the 'biotechnology wager' which we discussed in Chapter 1. In the context of research council plans, societal challenges are chosen in the light of broader social goals. For example, the BBSRC has three challenges in its 2011 *Delivery plan*: food security; industrial biotechnology and bioenergy; and enhancing lives and improving wellbeing.[430]

6.37 The use of grand societal challenges in today's policy discussions is heavily influenced by the Gates Foundation's 'Grand challenges in global health' initiative, launched in 2003 in collaboration with the US National Institutes of Health.[431] Following this initiative, such challenges became "a tool for mobilising an international community of scientists towards predefined global goals with socio-political as well as technical dimensions".[432] The challenges potentially allow for a more expansive social debate about funding priorities, and the views of the public are sometimes incorporated into their formulation, such as in the case of the UK nanoscience 'Grand Challenges'.[433] They also allow many different kinds of research (fundamental, strategic and applied) to fit under a single broad heading. Although we do see a familiar agenda of national economic competitiveness and technological leadership in the discussion of societal challenges, they can act to leaven the relentless influence on economic drivers that dominates research policy (see Chapter 7). They may also, however, be promoted by those with a vested interest in particular kinds of technology as a way of securing resources and other forms of support. Furthermore, there is a risk that meeting the challenges in prescribed ways can inadvertently and detrimentally come to define the criteria of 'success' in research (the 'tunnelling' problem we identified in Chapter 2[434]). We see the main bulwark against these dangers as being the cultivation of what we have labelled the 'virtue of enablement'[435] in institutional and procedural contexts and we therefore recommend that, **when framing science policy through societal challenges, a 'public ethics' approach should be taken to avoid an overemphasis on technological rather than social solutions to problems with substantial social dimensions**. Applying a public ethics approach (such as that which we set out in Chapter 4) to the consideration of research priorities can enable detailed scrutiny, rigorous critical analysis and extended peer review, as well as securing greater legitimacy, trust and public confidence in research directions.

The 'impact agenda'

6.38 Funding restrictions and the need for universities to increase revenue streams from elsewhere ('third stream' funding from organisations in the private, public and voluntary sectors, for example) have contributed to increasing demands placed on university researchers in the UK to

[428] See, for example, National Research Council (2009) *A new biology for the 21st century*, available at: http://www.nap.edu/catalog/12764.html.

[429] Beddington J (2009) *Food, energy, water and the climate: a perfect storm of global events?*, available at: http://www.bis.gov.uk/assets/goscience/docs/p/perfect-storm-paper.pdf. This is echoed with even more urgency by a joint paper presented at the UN Environment Programme's Governing Council meeting on 20 February 2012 by the 18 Blue Planet prize laureates, asserting that "humanity's behaviour remains utterly inappropriate for dealing with the potentially lethal fallout from a combination of increasingly rapid technological evolution matched with very slow ethical-social evolution" creating an "absolutely unprecedented emergency". See: Brundtland GH, Ehrlich P, Goldemberg J *et al.* (2012) *Environment and development challenges: the imperative to act*, available at: http://www.af-info.or.jp/en/bpplaureates/doc/2012jp_fp_en.pdf, p7.

[430] BBSRC (2011) *BBSRC delivery plan 2011-2015: maximising economic growth in the age of bioscience*, available at: http://www.bbsrc.ac.uk/web/FILES/Publications/delivery_plan_2011_2015.pdf.

[431] Omenn GS (2006) Grand challenges and great opportunities in science, technology, and public policy *Science* **314**: 1696-704.

[432] Brooks S, Leach M, Lucas H and Millstone E (2009) *Silver bullets, grand challenges and the new philanthropy*, available at: http://www.ids.ac.uk/files/dmfile/STEPSWorkingPaper24.pdf, p8.

[433] Kearnes M (2010) The time of science: deliberation and the 'new governance' of nanotechnology *Governing Future Technologies*: 279-301.

[434] See paragraph 2.33.

[435] See paragraph 4.52.

frame their research, both retrospectively and prospectively, in terms of 'impact'.[436] This reflects broader international trends. In the US, "broader impacts" are an essential criterion for assessing research proposals to the National Science Foundation, as specifically mandated by Congress.[437] In the EU's framework programmes, 'expected impacts' have always been given an explicit weight in proposal review and in successive programmes the types of impacts eligible to be considered has been tightened.[438]

6.39 The focus on impact represents a perfectly proper concern to ensure that research is often appropriately examined for its wider social and economic value, especially when that research is supported by public money, and to maximise the economic and wider public benefits of academic research. In the UK, the search for impact encompasses the encouragement of academic entrepreneurialism (which has been a feature of research policy since the 1980s, especially in the US[439]), the promotion of the importance of the university spin-outs through a series of government reports,[440] and the ascending influence of some successful role models. It also seeks to encourage the many other ways in which academic researchers interact with business, through collaborative research, consultancy and other routes.[441]

6.40 There are, however, several different concepts of impact, which frame the presentation of research in often subtly different ways, although economic value lies behind almost all. The main concepts of relevance to academic researchers in the UK are those implemented by the funding body for the universities, the Higher Education Funding Council for England (HEFCE), and the research councils.

6.41 Although the assessment of research impact is notoriously difficult,[442] particularly given the complexity of technology innovation systems and the range of disciplines to which it is applied, a retrospective assessment of impact underlies the Research Excellence Framework (REF),[443] the results of which will determine future university funding.[444] This provides a direct mechanism to shape institutional choices of public sector research direction in universities.

6.42 The forward-looking aspect of the impact agenda in the UK is implemented through the inclusion in research proposals of a section on 'pathways to impact'. Although interpreted by many as an (arguably futile) attempt to induce researchers to predict the future, it is more accurate to think of this as a way of attempting to modify the behaviour and values of

---

[436] The history of the Higher Education Funding Council for England or Department of Trade and Industry third stream funding is set out in Public and Corporate Economic Consultants and the Centre for Business Research (2009) *Evaluation of the effectiveness and role of HEFCE/OSI third stream funding*, available at: http://www.hefce.ac.uk/media/hefce1/pubs/hefce/2009/0915/09_15.pdf. At page 22, it is stated that: "The broad aim of all HEFCE/OSI third stream funding to date has been to enhance the direct and indirect economic benefits of HE, through embedding a culture and capacity within institutions that support the transfer and exchange of knowledge between HE, business and the wider community."

[437] National Science Foundation (2011) *National Science Foundation's merit review criteria: review and revisions*, available at: http://www.nsf.gov/nsb/publications/2011/meritreviewcriteria.pdf. The America COMPETES Reauthorization Act of 2010 lists eight goals to be met under this heading: increased economic competitiveness of the United States; development of a globally competitive STEM workforce; increased participation of women and underrepresented minorities in STEM; increased partnerships between academia and industry; improved pre-K–12 STEM education and teacher development; improved undergraduate STEM education; increased public scientific literacy; and increased national security.

[438] Holbrook JB and Frodeman R (2011) Peer review and the ex ante assessment of societal impacts *Research Evaluation* **20**: 239-46; the extension of the impact agenda has drawn equally robust resistance in some quarters; see: Jump P (2012) ERC rejects 'impact agenda' *THE* 8 March, available at: http://www.timeshighereducation.co.uk/story.asp?storycode=419276.

[439] Slaughter S (1993) Beyond basic science: research university presidents' narratives of science policy *Science, Technology & Human Values* **18**: 278-302.

[440] For example: Sainsbury D (2007) *The race to the top: a review of Government's science and innovation policies*, available at: http://www.hm-treasury.gov.uk/d/sainsbury_review051007.pdf.

[441] Abreu M, Grinevich V, Hughes A and Kitson M (2009) *Knowledge exchange between academics and the business, public and third sectors*, available at: http://www.cbr.cam.ac.uk/pdf/AcademicSurveyReport.pdf.

[442] See, for example, Grant J, Brutscher P-B, Kirk SE, Butler L and Wooding S (2010) *Capturing research impacts: a review of international practice*, available at: http://www.rand.org/content/dam/rand/pubs/documented_briefings/2010/RAND_DB578.pdf.

[443] The 'Expert Panels' of the REF will begin assessing submitted research in 2014. The work to be assessed will be that performed from 2008-2009. See: REF2014 (2012) *Timetable*, available at: http://www.ref.ac.uk/timetable.

[444] REF2014 (2012) *Background*, available at: http://www.ref.ac.uk/background.

researchers, by priming them to think about how they might increase the 'utility' of their research in terms of who the onward users of that research might be (and, indeed, to build anticipatory links with them).

6.43 This may have the effect of reinforcing, within the research community, an external notion of utility, albeit one that may be narrower and more elusive than measures of utility found within research itself, as we see in the conspicuous emphasis on economic impact in relevant policy documents. A second consequence, of course, may be not that research becomes better at generating utility (however this is defined), but that researchers become better at manipulating the system, particularly if the endpoints are remote and the pathways unclear, and there is little likelihood of attracting a penalty for doing so. Such a process may therefore produce an *illusion* of administrative control while actually making the process of research more constrained, and less flexible and creative.

6.44 The identification by researchers of the distributaries of wider value for their research provides channels for the appraisal of ethical, legal and social implications of research. It also facilitates policy 'impact assessment' (adapted into a variety of administrative forms). By nature these tend to give concrete form and value to impacts and displace more open social appraisal of biotechnologies. The tendency to simplification and concretisation of the concept of impact may also become exacerbated and consolidated by bioethicists and others, whose modes of argument often involve pointing to exaggerated, absurd or intolerable consequences.[445] This may result, for example, in an undue focus on speculative scientific claims or dystopian scenarios as standard reference points within the discourse surrounding biotechnologies, driving apart scientific practice and the discourse on that practice, and thereby creating opportunities for mistrust and disappointment.[446]

6.45 Some have argued that such discursive interactions instigate a 'promise-requirement cycle', where scientists, funders and others articulate technological possibilities, signal opportunities, that give rise to promises of possible future states of affairs which, if accepted, result in the provision of resources as well as the imposition of additional requirements.[447] This cycle prompts speculation and concerns about future worlds, which in turn trigger further promises and requirements.[448] The dynamics of such institutionalised processes entail a very pertinent danger of escalating expectations driven partly by the competitive nature of research funding.

6.46 The causes of dissonance between the discourses on impact and the prospects of research are not solely or principally the responsibility of researchers, but arise in the encounter with the broader system of research funding, policy and expectant users, critics and beneficiaries on one hand, and the realities and uncertainties of research and innovation systems on the other. The necessity of engaging in competition for funding from various sources nevertheless places researchers in an invidious position. We conclude that there is a need for institutional systems to be designed better to embody and instil the virtues of public reasoning, accountability, candour, and caution and recommend in particular that **public systems for the allocation of research funding should be designed to avoid encouraging researchers to overstep the bounds of their competence when assessing the impacts of their research in non-research contexts**.

[445] The 'slippery slope' argument, for example, is a common trope in bioethics of new technologies. See: Swierstra T and Rip A (2007) Nano-ethics as NEST-ethics: patterns of moral argumentation about new and emerging science and technology *Nanoethics* **1**: 3-20.

[446] Nordmann A (2007) If and then: a critique of speculative nanoethics *Nanoethics* **1**: 31-46. In addition, in Borup M, Brown N, Konrad K and van Lente H (2006) The sociology of expectations in science and technology *Technology Analysis & Strategic Management & Organizational History* **18**: 285-98, the authors describe the dynamics of hype and disappointment and the functioning of promising in securing commitment to technological futures.

[447] See, for example, van Lente H and Rip A (1998) Expectations in technological developments: an example of prospective structures to be filled in by agency, in *Getting new technologies together*, Disco C, and van der Meulen B (Editors) (Berlin: Walter de Gruyter).

[448] Rip A (1997) A cognitive approach to relevance of science *Social Science Information* **36**: 615-40.

Public expectations and responses

6.47 Although the global scientific enterprise as a whole has a certain amount of self-sufficiency and a great deal of self-confidence, it is not isolated from or uninfluenced by the views of wider society. In emerging biotechnologies, opposition to forms of agricultural biotechnology (in Europe), stem cell research (in the US), and the use of animals for experiments, have all had a significant effect on the direction of research. In some cases researchers' perceptions of what the public think may be as important as what those views actually are. In the context of nanotechnology, for example, the name "nanophobia-phobia" has been given to exaggerated concerns amongst the research community about public reactions to nanotechnology.[449] On the other hand, the exposure of researchers to positive views from the public about the importance of their research, for example in biomedical research through the influence of patient groups and research charities, can shape research agendas and contribute to a sense of the value and urgency of biomedical research.

Global context

6.48 The culture of science is strongly transnational, but nonetheless scientists work in distinct locations subject to differing national environments. Different countries have different funding climates and funding priorities, though these inevitably influence each other. Public attitudes to different aspects of emerging biotechnologies have strong national differences, reflecting the divergent cultural and political histories of different nations.[450] Formal legal and regulatory structures necessarily have a territorial basis. Researchers, on the other hand, are often in a position to relocate to a different country if that environment is more congenial to their research. This leads to the very real possibility of a kind of regulatory arbitrage, which can be perceived to limit the ability of an individual nation to maintain a policy or regulatory stance that diverges strongly from world norms.

Influence *of* researchers

6.49 Researchers are undoubtedly subject to many external pressures and influences but they nevertheless play a very important role in setting the agenda for emerging biotechnologies. They not only create new knowledge but, by communicating the results of their research and their aspirations for where it might lead, they create the expectations that inform the decisions of policy makers and investors, among others. Subpopulations of researchers control, through peer review, what research is published and where, and, through the status hierarchy of scientific journals, the level of importance attached to particular pieces of research and particular fields and sub-fields. Through the peer review of research proposals, researchers also control funding at the micro-level of individual research projects; however, they also influence the strategic directions of funders through advisory committees and other forms of formal and informal consultation, advice and participation.

Researchers as communicators

6.50 Researchers devote a significant amount of their time communicating their research to a number of different audiences, such as their peers and funders, and the media.[451] These various communications have different aims. When we consider how knowledge of emerging biotechnologies is presented in the domain of biotechnology and the way these representations feed back into the science and policy domains, we should begin by attending to these different ways that researchers communicate. To the extent that discourse around emerging biotechnologies constitutes an economy of promises, where visionary and speculative claims

[449] Rip A (2006) Folk theories of nanotechnologists *Science as Culture* **15**: 349-65.
[450] Jasanoff S (2005) *Designs on nature: science and democracy in Europe and the United States* (Princeton, New Jersey: Princeton University Press).
[451] See: Peters HP, Brossard D, de Cheveigné S *et al.* (2008) Interactions with the mass media *Science* **321**: 204-5.

are necessary to attract interest and investment, researchers provide most of the raw materials for that economy.[452]

6.51 The messages that researchers communicate are not invariable and are often tailored to the capacities and requirements of those with whom they communicate. Nevertheless, despite the involvement of scientists in the public understanding of science movement and, more latterly, in public engagement,[453] There is evidence that scientists who communicate with the public may still be failing to attend adequately to the needs of their audiences or to tailor their messages to them.[454] Either way, whether the messages are adapted by the scientists or not, the communication of technical information outside its native technical discourse involves a reframing, either of the message that is sent (by the earnest scientist-communicator who tailors their message to the audience), or of the information that is received (by the lay person struggling to find a way of making sense of the uncompromising technical information in terms with which they are more familiar). It is therefore worth considering the complex network of communication about biotechnologies in which researchers participate in order to appreciate the difficulties of maintaining the consistency and integrity of message about their research. Furthermore, because researchers' communications about biotechnologies are often intended to secure an effect rather than merely to express the truth of a proposition, these are likely to vary depending on the audience or the effect sought.

6.52 Researchers communicate with each other (i.e. to people in the same field) to report results, debate interpretations and establish priority. They communicate with policy makers and funders to make the case for the continued funding of their area or to establish the importance of new disciplinary formations (such as systems biology or synthetic biology). Researchers also communicate with the general public, both directly and through the press offices of universities and journals. Sometimes they are involved in 'public science education' or even as expert witnesses in deliberative engagement activities. More often their communications are further filtered and propagated by journalists and broadcasters, including both science specialists and generalists (see Chapter 5).

6.53 Some of the communication researchers engage in is concerned with reporting the immediate results of their research groups, but this is often set in the context of grander narratives or references to popular images, as we discussed in Chapter 2. A balance clearly has to be struck here between using familiar concepts to get across difficult points and distorting complex messages, particularly when these communications may take on an independent life and may be recycled almost indefinitely in a variety of different contexts. Researchers in biotechnology must acknowledge the public nature of their work and the public interest in it. The virtue of public reasoning goes beyond openness and candour because it entails researchers assuming a responsibility, having carried out research in which there is a public interest (and which furthermore may have relied on public funding) to account for it in public discourse. Therefore **those engaging in public discourse should not only accept responsibility for the factual accuracy and completeness of information they present but also use their best endeavours to ensure, through their continued participation in this discourse, that it is appropriately qualified and interpreted when represented by others**. There are two implications of this: firstly, that those relying on research evidence in other contexts should provide opportunities for ongoing participation of the researchers whose findings they use; second that researchers themselves should not only present complete relevant data (not only data favourable to one side of the argument) but, in doing so, be prepared to engage in discourse about science with the objective of developing understanding of science and the ambitions of scientists (their own as well as their interlocutors') rather than merely communicating scientific findings.

---

[452] Brown N (2003) Hope against hype: accountability in biopasts, presents and futures *Science Studies* **16**: 3-21; Hedgecoe A and Martin P (2003) The drugs don't work: expectations and the shaping of pharmacogenetics *Social Studies of Science* **33**: 327-64.

[453] For example, initiatives such as those of the Cafés Scientifiques, the British Science Association (formerly the British Association for the Advancement of Science), the RCUK Beacons for Public Engagement or the Royal Institution's Science Media Centre.

[454] Corley E and Scheufele D (2010) Outreach gone wrong? When we talk nano to the public, we are leaving behind key audiences *The Scientist* **24**: 22-9.

6.54 Alongside the communication activities of professional researchers, one group of 'unofficial', or amateur, scientists that has received a large amount of attention in the press is the DIYbio movement.[455] Related to this is the 'bioart' movement, in which artworks are created from, amongst other things, genetically modified organisms and artefacts.[456] It is difficult to assess the full extent of the activities of amateur scientists, and their levels of expertise. However, the symbolic importance of these interventions is likely to be as great as their actual potential to create new developments in biotechnology, insofar as they add to the impression of emerging biotechnologies growing in power and accessibility at the same time as they evade the conventional controls and constraints on the development of high technology.

Researchers as gatekeepers of knowledge

6.55 The most important mechanism through which researchers control the production of knowledge is the peer review process. This has built-in limitations, since scientific and technical considerations necessarily dominate: its weakness in assessing interdisciplinary proposals has been shown in an analysis of the UK's research assessment exercises.[457] It is also difficult to judge potential impact outside of academia, both positive and negative.[458]

6.56 In the design of research approaches (such as universities, institutes, firms, competitions, open source, biotechnology clusters) and their connections with developers, innovators and users, researchers authorise and legitimise certain types of knowledge and not others. They also control who counts as a credible contributor to the scientific work (for example, DIYBio groups are excluded from synthetic biology events such as the International Genetically Engineered Machine (iGEM) competition, unless they are affiliated with an academic institution, on the grounds that iGEM participants must work under the safety rules of an institutional laboratory).[459] This puts researchers in a powerful but, in effect, unaccountable, or self-regulating, position. To cultivate accountability here is not to establish a disciplinary consensus but precisely to engage with wider society about these questions of legitimacy.[460]

Researchers as advisors

6.57 Finally, the most obvious way in which scientists influence the development of emerging biotechnologies is through their roles as policy makers and policy advisors to government and government agencies. In an environment in which policy may be driven excessively by unsupported claims of economic impact, business and industry voices may have disproportionate influence. The involvement of scientists in policy making may yield benefits in terms of their tenure, expertise and appreciation of the methodological value of scepticism. Balanced against this, however, are risks of over-reliance on particular types of expertise and a greater danger of reinforcing perspectives or framings in wholly technical terms.

6.58 Privileging technical expertise in advisory contexts may mean that greater weight is given to 'harder' scientific evidence in evidence-based policy making, i.e. there may be confusion between the idea of evidence that is scientifically more robust and evidence that is more important to the decision to be made ('counting what can be counted rather than what counts').

---

[455] Alper J (2009) Biotech in the basement *Nature Biotechnology* **27**: 1077-8; Ledford H (2010) Life hackers *Nature* **467**: 650-2.
[456] Kac E (Editor) (2007) *Signs of life: bio art and beyond* (Cambridge, Massachusetts: MIT Press).
[457] Martin B and Whitley R (2010) The UK research assessment exercise, in *Reconfiguring knowledge production: changing authority relationships in the sciences and their consequences for intellectual innovation*, Whitley R, Gläser J, and Engwall L (Editors) (Oxford: Oxford University Press).
[458] Rip A (2003) Societal challenges for R&D evaluation, in *Learning from science and technology policy evaluation: experiences from the United States and Europe*, Shapira P, and Kuhlmann S (Editors) (Cheltenham: Edward Elgar Publishers).
[459] See: Anonymous (2009) iGEM closes doors to amateurs, on *DIYBio* [internet blog] 10 April, available at: http://diybio.org/2009/04/10/igem-closes-doors-to-amateurs and http://igem.org/Main_Page.
[460] See, for example, the sensitivity of the question of legitimate science in the case of 'climategate' in which, despite broad scientific consensus, there was still intense public suspicion about the internal machinations of science. See: Carrington D (2011) Q&A: 'Climategate' *The Guardian* 22 November, available at: http://www.guardian.co.uk/environment/2010/jul/07/climate-emails-question-answer.

There is also a danger of entrenchment of scientific advice, with a narrow range of expertise repeatedly drawn upon in policy contexts (partly because officials who seek scientific advice have to turn to experts to find out who the appropriate experts are, but they need an expert to tell them which expert to ask, and so on, so that they are caught in a pernicious regress of dependence on a potentially limited range of expertise). Where these processes occur in established networks or behind closed doors, any judgment can become self-reinforcing. To avoid this problem, or the appearance of this problem, we recommend that **in all cases in which technical advice is sought by policy makers there should be a demonstrable attempt to avoid sole reliance on a limited range of established experts in particular fields**. This balance should be achieved through a broadening of participation in discourse (rather than through the more earnest selection of unimpeachably authoritative individuals).

6.59 Scientists involved in policy advice may be required to contribute to discussion of issues, such as implementation and scale-up that fall outside their direct area of expertise. In these situations there may be ambiguity over whether they are speaking as scientists, as policy makers, or, indeed, as citizens. Additionally, scientific advice is important to policy making but it is not all that policy makers have to consider. The emphasis on evidence-based policy making can sometimes place a premium on scientific advice and especially on the interpretation of quantitative data, and such data are, as we have seen, subject to selectiveness and interpretive ambiguity. On the other hand, the expectation that policy is framed in terms of scientific evidence can also lead to misunderstanding when broader social responsibilities of policy makers figure strongly, which is not helped by the mission creep of scientific advisory committees within government into giving political and ethical advice.[461]

6.60 While scientists are not exempted from conflicts of interest and partisanship, there is no reason to think they are more prone to this than other groups such as industrialists or financiers.[462] But the privilege granted to scientific evidence in policy making means that scientists involved in giving policy advice have a particular responsibility to exercise self-restraint and vigilance to avoid projecting a false sense of 'scientific certainty'.[463] Nevertheless, they will clearly have an interest in their own work and its value, although this need not betoken a deliberate, instrumental distortion of priorities but instead simply reflect their greater insight into and commitment to their own research. Equally, therefore, there should be more licence for researchers candidly to assert their own convictions that their work promotes public good beyond simple economic benefit.

Extending the boundaries of research

6.61 As well as researchers participating in different discourses of, and also as, policy makers and policy advisors, we see groups such as social scientists, lawyers, patients, and even artists and designers, becoming involved in scientific research. In recent years, these 'others' have become associated with many new fields, such as nanotechnology, stem cell research, and neuroscience, and social scientists are becoming a required component of synthetic biology research programmes around the world.[464] Because of such initiatives, new relations between science, technology and society are being created, which provide new spaces for intervention.[465] In certain cases, and owing to the interdisciplinary nature of biotechnologies, these have been formalised in institutes,[466] although the advantages of flexibility can be found in the *ad hoc* 'situatedness' of 'cooperative research'.[467] It is consistent with the virtue of

[461] We discuss this issue further in Chapter 7. Experiences in policy making concerning GMOs and drug classification present examples of the contrasting expectations about the role of scientific evidence in policy making.
[462] On scientists' role as policy makers and the influence of their own ideologies, see: Jasanoff S (1994) *The fifth branch: science advisers as policymakers* (Cambridge, Massachusetts: Harvard University Press).
[463] John S and Lewens T (2010) *The universal ethical code for scientists and the 'crisis of trust in science': report to the Science and Trust Working Group*, available at: http://interactive.bis.gov.uk/scienceandsociety/site/trust/files/2010/03/Ethical-Codes-and-Trust-16-Feb-20101.pdf.
[464] Calvert J and Martin P (2009) The role of social scientists in synthetic biology *EMBO Reports* **10**: 201-4.
[465] Webster A (2007) Crossing boundaries social science in the policy room *Science, Technology & Human Values* **32**: 458-78.
[466] Such as the collaboration that existed between the Imperial College London and the BIOS Centre, King's College London in the Centre for Synthetic Biology and Innovation, see: http://www3.imperial.ac.uk/syntheticbiology.
[467] For example, the Co-operative Research on Environmental Problems in Europe (CREPE) project; see: http://crepeweb.net.

enablement and public reasoning that, particularly given the influence of researchers outside the research context, the boundaries of this context should be broadened to enable technical framings and sources of normativity to be counterbalanced within the research context rather than externally to it, where they might already circumscribe decision making. This should not be left to the integrity of individuals but should be supported by systems.

Conclusion

6.62 In this Chapter we have considered the influences *on* researchers that inform how their influence may be co-opted or directed and the role *of* researchers in shaping emerging biotechnologies. We have suggested that, both among individual researchers as well for researchers in general, there is a 'function creep' from research into policy making that heightens the influence of technical framings in setting the conditions for biotechnologies generally. Perhaps the most characteristic feature of researchers' involvement, arising from the 20th Century specialisation and professionalisation of scientific research, is their commitment to individual technologies: consulting any researcher is unlikely to produce a balanced reflection on a range of alternative technologies that might potentially address a given social objective. In the next Chapter we consider the questions that arise for policy makers in contemplating selective support for biotechnologies in relation to social objectives, and the influence of research policy on emerging biotechnologies.

Chapter 7

Research and innovation policy

Chapter 7 - Research and innovation policy

Chapter overview

In this Chapter we examine the ways in which research policy shapes the emergence of biotechnologies, focusing mainly on the UK and on the 21st Century. We conclude that the UK has no policy for emerging biotechnology generally as distinct from its policy for technology, and that policy for particular emerging biotechnologies (such as regenerative medicine) stands in for other life sciences. We find that technology policy, including in the life sciences, has become increasingly framed by the single dimension of economic growth, even to the apparent cost of improving health and well-being (at least in terms of attention given to these in relevant documents), and that even policy for biomedical technologies is framed in this way, except the policy of charitable funders who continue to have a substantial role.

We identify and discuss a number of assumptions that arguably underlie UK research policy and find that they are not well founded or well argued. For example, the commonplace notion that the UK is good at research but poor at commercialisation is not borne out by the evidence; the argument that conditions are in place for funding of biotechnology research to feed through into national prosperity is not well made; that the importance of biotechnology to the public good and its likely impact may be hugely overstated; the supposed 'Haldane principle' that the direction of basic research should be directed by researchers rather than politicians or industry is more honoured in the breach than the observance, directed as it is to securing 'commercialisable' innovations.

We conclude, as we did in Chapter 5, that the discourse on research policy has become detached from the realities of research and social values, and that that there is a need to reframe public research policy in a coordinated and less piecemeal way through an engagement with a broader range of societal interests.

Introduction

7.1 This Chapter is concerned with research policy, in particular, with the principles and assumptions behind public policies for research, as well as the policies of relevant charitable bodies. The policies of commercial businesses involved in biotechnology research will be dealt with separately, in Chapter 9. In the very crudest characterisation, public policy has two main levers with which to control research: *facilitation* using money obtained from general taxation and *inhibition* through legislation and regulation. We will address the question of regulation separately in the next Chapter; here we are mainly concerned with how funding is channelled to different institutions and projects of research, and withheld from others. Institutional biotechnology research is a significant public expenditure and this fact alone, as we noted in Chapter 4, brings it within the scope of the public interest.[468] Although our focus here will be principally on the UK, many of the issues explored are common to other countries, and policy is treated within an international context. Indeed, it is of ethical significance that the major impacts of research policy may well occur beyond the bounds of the jurisdiction to which the policy applies.

Policies for biotechnology

7.2 Although biotechnology has long been a central theme in UK research policy, 'emerging biotechnology' is not a term commonly used in official literature, either as an organising principle in policy, or as a budget category. Nevertheless, a great many more general policies and processes are relevant to research in emerging biotechnologies and we discuss these along with more strategic measures aimed at specific examples of emerging biotechnologies. In particular, in recent UK policy documents, emphasis has been placed on two areas that would currently qualify for this description: synthetic biology and regenerative medicine.

7.3 Our particular focus here is on how policy engages, or could engage, with the social and ethical concerns in which we are interested. We find very limited discussion of these issues, excepting the particular case of research ethics,[469] by both Government and charities, even when

[468] See paragraph 4.9.
[469] That is, ethics relating to the *conduct* of research rather than nature and selection of research.

research policy is directed to achieving impact on medical practice, for example. There is, however, a great deal of discussion of economic matters, which we will take up in a way that might seem surprising in a Report of this nature. However, this is important for two reasons. Firstly, because of the significance attached to economic considerations, social and ethical aspects are rendered much less visible. In the UK at least, despite occasional references to 'health', 'quality of life' and 'sustainability', discussion of innovation and technology in Government publications is framed very largely in terms of 'competitiveness' and 'economic growth'. (Medical charities are, for obvious reasons, concerned with health rather than economic competitiveness.) This is mirrored in the prominent role given to industry personnel in official bodies but it is important to note that all research policies are framed in this way, not merely those concerned with industry. Secondly, this focus on economic growth and competitiveness is itself a matter of choice and the dominance of this framing could – and, indeed, *should* – be challenged through public discourse ethics. Indeed, many of the economic arguments are arguably not as well-grounded as they appear to be and, even if they were, we would argue that they should not necessarily trump other considerations.

Investment in emerging biotechnologies

7.4 Biotechnology has been a concern of UK research policy for decades. The Spinks Report of 1980 led to the Medical Research Council (MRC) and the Science and Engineering Research Council establishing substantial biotechnology research programmes, and the (then) Department of Trade and Industry establishing a biotechnology directorate in November 1981.[470] By 1985, 40 small biotechnology firms had been established in the UK, possibly more than in all other countries of Europe put together.[471] The Biotechnology and Biological Sciences Research Council (BBSRC) was established in 1994. The Cambridge Laboratory of Molecular Biology (LMB) was at the centre of the effort to foster innovation, and some spin-outs from this enjoyed notable success; for example, Cambridge Antibody Technology and Domantis were later acquired by large pharmaceutical firms.[472] As a result MRC and LMB scientists received substantial royalty income, outstripping the value of the MRC grant that supported the initial work.[473]

7.5 Despite this interest in biotechnology research and development (R&D), 'biotechnology' is not a category used for reporting research expenditures for the public or private sectors. We can, however, reach some broad conclusions that are significant for policy. The first is that terminology can mislead: for example, 'biotech' firms are not the main funders of biotechnology R&D.[474] In fact, pharmaceutical firms outspend biotech firms even on biotechnology R&D.[475] It should also be noted that much biotechnology is outside medicine and it is likely that here, too, established large firms spend more than biotech firms. Furthermore, the private sector outspends the public sector on R&D. Although this cannot be established directly for biotechnology, it is likely to be the case for *medical* biotechnology given that the total UK public sector spend on health related R&D was reported to be approximately £1.5 billion in 2008/2009,

[470] See: Advisory Council for Applied Research and Development, Royal Society and Advisory Board for the Research Councils (1980) *Biotechnology: report of a Joint Working Party* (London: HMSO).

[471] Although also approximately one-tenth of that in the US. See: Yoxen EJ (1985) Government promotion of biotechnology *Physics in Technology* **16**: 234-41.

[472] Cambridge Antibody Technology was acquired by AstraZeneca and Domantis by GlaxoSmithKline, both in 2006. See: Attwood K (2006) GSK snaps up Domantis to move into biotech field *The Independent* 9 December, available at: http://www.independent.co.uk/news/business/news/gsk-snaps-up-domantis-to-move-into-biotech-field-427735.html; BBC News Online (2006) *AstraZeneca to buy CAT for £702m*, available at: http://news.bbc.co.uk/1/hi/business/4771615.stm. We return to the economics of biotechnology acquisitions in Chapter 9. See paragraph 9.8 to 9.12.

[473] "By 2005, the annual revenues from LMB inventions – £20 million, with the lion's share stemming from the Winter patents – exceeded the total MRC block grant to the LMB…In 2008 the annual income had risen to £70 million." de Chadarevian S (2011) The making of an entrepreneurial science: biotechnology in Britain, 1975-1995 *Isis* **102**: 601-33.

[474] An editorial in *Nature Biotechnology* notes: "…much, if not most, of the biological products and biological techniques now resides outside of the group of independent public companies that we survey. Pharma spends $65 billion a year on R&D, 25-40% of it either devoted to biological products or using the techniques of biotech." Nature Biotechnology editorial (2010) Wrong numbers *Nature Biotechnology* **28**: 761.

[475] Hopkins M (2012) *Emerging biotechnologies: can we find out who funds R&D and what they support?*, available at: www.nuffieldbiothics.org/emerging-biotechnologies-evidence-reviews, p6.

while biomedical charities were reported to have spent £1.1billion, and private industry claims to have invested £8.9 billion.[476] We may therefore conclude, albeit cautiously, that the main centres of decision-making where support for biotechnology is decided are:

- a handful of large pharmaceutical and industrial firms;
- Government bodies concerned with research (principally research councils);
- medical charities; and
- a large number of dedicated biotechnology firms.

While public policy needs to take account of the research policy of private sector organisations, we do not address the latter directly here, but instead address the role of such organisations separately in Chapter 9.

Strategic orientation of R&D policy

Evolution of strategic and interdisciplinary advice

7.6 The UK's advisory framework for biotechnologies underwent a structural reorganisation following a comprehensive review in May 1999, at a time when the major focus of biotechnology policy was genetics, as it was then understood.[477] The review concluded that the arrangements for regulating individual products and processes operated satisfactorily but that there was insufficient strategic clarity as a result of fragmented advisory committees that lacked transparency and responsiveness to social and ethical issues that were of concern to the public.

7.7 The subsequent reorganisation saw a number of *ad hoc* committees consolidated under a smaller number of broad cross-departmental strategic functions. These functions were provided by, for genetically modified foods, the Food Standards Agency (FSA, established by the Food Standards Act 1999) and two new bodies: the Human Genetics Commission (HGC) and the Agriculture and Environment Biotechnology Commission (AEBC). These bodies were established to operate at a high level and appointments to their boards had the significance of major public appointments (even though they were, initially, within the gift of Ministers). The membership of these bodies was deliberately diverse[478] and they were given the specific role, as well as resources, to deliberate broadly and openly, to interact with the public, and to provide independent advice to Ministers across Government – even when such advice was not sought – on the 'big picture'. However, eventually the vision became somewhat more domesticated and problem-focused: the HGC concentrated on elaborating implications of genetic testing identified in its first Report, *Inside information*, and exploring approaches to public involvement in policy making at an increasing arm's length from Government; the FSA continued to operate principally an executive agency that internalised certain advisory functions, and the AEBC was wound up in 2005.

7.8 In 2010, a review of arm's length bodies was undertaken,[479] ostensibly brought about by the financial crisis and the need for greater efficiency in Government agencies. Following this

[476] Ibid, p16, citing Morgan Jones M and Grant J (2011) *Complex trauma research in the UK: a rapid review of the funding landscape*, available at: http://www.rand.org/content/dam/rand/pubs/documented_briefings/2011/RAND_DB613.pdf.

[477] Cabinet Office (1999) *The advisory and regulatory framework for biotechnology: report from the Government's review*, available at: http://webarchive.nationalarchives.gov.uk/+/http:/www.berr.gov.uk/files/file14498.pdf.

[478] Though all expert in some way, the disciplinary diversity of membership is consistent with the findings of a 1999 MORI public survey commissioned to support the review. When asked who they felt should be involved in making decisions on their behalf in the regulation of the biological sciences, respondents placed advisory bodies comprising experts and people with different viewpoints higher than central Government itself. See generally: MORI (1999) *The public consultation on developments in the biosciences: A MORI report investigating public attitudes to the biological sciences and their oversight*, available at: http://webarchive.nationalarchives.gov.uk/+/http://www.bis.gov.uk/files/file14580.pdf.

[479] In the Coalition agreement, the commitment that "We will reduce the number and cost of quangos" comes, as a distinct plank of policy, under the heading 'Deficit reduction'. HM Government (2010) *The Coalition: our programme for government*,

review, in 2012 the HGC was closed down, mirroring the fate of the AEBC. The future of the FSA was also put into question. The 'successor' to the HGC is the Emerging Science and Bioethics Advisory Committee, which follows the model of a scientific advisory committee rather than a strategic advisory body in that it is sponsored by the Chief Scientific Adviser for the Department of Health in England, and its terms of reference are, unsurprisingly, restricted to health.[480] Nevertheless, it is the "main UK advisory body on the wider implications of developments in bioscience and its impact for health"[481] and provides a forum to consider and develop coordinated advice across the wider science, health and academic communities to help set priorities in response to new developments.

7.9 In light of the decline of overarching strategic advisory bodies, two contractions are discernible. Firstly, a reduction in the importance of interdisciplinary deliberation on issues within biotechnology policy producing interdisciplinary framings of the issues; secondly, a withdrawal of policy discussion from sites where public access and participation is possible, leading to a reduction in the range of voices and the type of considerations that have an audience at the highest levels of policy making. These developments therefore arguably represent a decline in the institutionally recognised sites and channels for public discourse ethics to bear upon national policy in relation to emerging biotechnologies.

The growth of the 'growth agenda'

7.10 There has been a very important change in the ecology of UK research over the past four decades. Aside from moving from a very research intensive economy in the 1960s to one with a research intensity well below that of many other economies, there has been an important change in public funding of research, namely the reduction in departmental civil R&D expenditure. This reduction has meant that approximately one half of all public R&D expenditure is spent through the Higher Education Funding Councils and the research councils.[482] We should recall, however, that there is no single Government research policy, and that in each of the sectors research policy is made on a different basis with different aims in mind.[483] However,

available at: http://www.direct.gov.uk/prod_consum_dg/groups/dg_digitalassets/@dg/@en/documents/digitalasset/dg_187876.pdf, p16.

[480] The distinction between advice and administration developed in a way that was somewhat less clear-cut than the high level policy documents suggested. First, a host of Scientific Advisory Committees (SACs) of experts (usually convened by officials), with closely defined remits, continued to exist for all departments. Almost all Government departments maintain a number of SACs. Although nominally offering scientific expertise, these may also creep into offering ethical advice, an idea that may be encouraged by (although not discharged by) the presence of 'lay' members on the committees. Consequently their function is often ambiguous and vulnerable to mission creep in at least two dimensions: (1) from advice to oversight and regulation; (2) from strictly scientific advice, which always needs to be interpreted in its relevance to public policy, to advise on broader implications. Although established by departments, SACs are loosely marshalled by the Government Office for Science headed by the Government Chief Scientific Adviser (who advises the Prime Minister rather than a BIS Minister). The Government Office for Science produces a Code of Practice that is supposed to reinforce the independence of these committees. The other main source of advice comes from arm's length bodies that flourished in the 1980s. Executive non-departmental public bodies such as Human Fertilisation and Embryology Authority (HFEA – the statutory regulator of assisted conception and human embryo research) have a statutory function to provide advice to the Secretary of State upon request, but also have significant discretionary powers to make 'regulatory' policy within the framework set out in legislation. The HFEA is an interesting case, as it was established as an 'ethical regulator' (unlike the majority of health regulators whose purpose was largely to protect the interests of service users by providing an external product/procedure approval and quality assurance function). In other words, its decisions were guided – in part, but necessarily – by reflection on a set of principles abstracted from a negotiated (but shifting) public settlement on where moral lines should be drawn, rather than simply by the need to provide reasonable levels of protection for patients. Part of the HFEA's role is to track this shifting settlement and respond to it as long as it appears to remain within the parameters agreed by Parliament. The Government could also draw advice from more apparently 'administrative' agencies such as the MHRA.

[481] Department of Health (13 March 2012) *Department seeks chair and members of science and bioethics advisory committee*, available at: http://www.dh.gov.uk/health/2012/03/esbac.

[482] In 2010, of UK public funds spent (in cash terms) on R&D, the Government spent £3.2 billion, the research councils £2.9 billion, and the HEFC £2.3 billion. The Ministry of Defence spent approximately £1.8 billion. See: Office for National Statistics (2010) *Gross domestic expenditure on research and development, 2010*, available at: http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-257461, Table 1; Defence Analytical Services and Advice (2010) *UK defence statistics*, available at: http://www.dasa.mod.uk/modintranet/UKDS/UKDS2011/pdf/c/ukds.pdf, Table 1.7.

[483] By 'sectors', in this context, we mean not only the public, private and charitable sectors but also the different Government departments and the research councils.

discussion of research policy is often presented, not least by Government, as if it were one policy, particularly through the emphasis on the connection of research and growth, ignoring the diversity of agencies and policies. Thus, while the particular principles that might or might not apply to research council policy should not be conflated with principles that might or might not exist for different parts of Government research policy, it is clear that research councils are expected to play a significant role in the generation of economic growth, a role which would once have centred on civil departments which themselves had responsibilities for active industrial policies in their sectors.

7.11 The promotion of economic growth has, in fact, featured quite centrally in the aims of research councils for many years. In the last Labour Government, Treasury policy was set out in the *Science and innovation investment framework 2004-2014*. The opening sentence of this document arguably sets the tone for what followed, stating: "Harnessing innovation in Britain is key to improving the country's future wealth creation prospects."[484] The aim was, over ten years, to increase R&D intensity in the UK economy (that is, the gross domestic expenditure on R&D as a proportion of gross domestic product (GDP)) from approximately 1.9 per cent to 2.5 per cent.[485] This initiative was based on the assumption that increases in public sector R&D spending would lead to increases in private sector R&D spending. These increases in private sector spending have not, however, been forthcoming.[486] Funding allocation for research councils increased by about 26 per cent between 2004 and 2008,[487] and there were also increases in HEFCE research funds. However, the research intensity of the economy did not increase significantly: research intensity was 1.68 per cent in 2004 and 1.86 per cent in 2009 (in 1986, it was 2.22 per cent);[488] there was barely any growth in real absolute expenditure on R&D by the private sector, which fell from 1.17 per cent of GDP in 2001 to 1.12 per cent in 2009 (it was 1.05 per cent in 2004[489] and 1.53 per cent in 1986.)[490] Despite sobering experiences of this kind, however, the EU has recently agreed a new set of research intensity targets with the objective of delivering economic growth.[491]

From research to innovation

7.12 While the policy focus on simply increasing research intensity has borne little fruit, the ambition to increase the economic impact of the UK research base through innovation processes has gained greater attention, particularly as pressure on public finances has increased. The Technology Strategy Board (TSB), established in 2007, has as its goal "to accelerate economic growth by stimulating and supporting business-led innovation."[492] The policy set out in the document *Innovation and research strategy for growth* makes this emphasis clear.[493] The

[484] Department for Innovation, Universities and Skills (2004) *Science and innovation investment framework 2004-2014*, available at: http://www.hm-treasury.gov.uk/d/spend04_sciencedoc_1_090704.pdf, p5.
[485] Ibid, p7.
[486] HMRC (2004) *Spending review*, available at: http://webarchive.nationalarchives.gov.uk/+/http:/www.hm-treasury.gov.uk/spending_sr04_science.htm.
[487] Department of Trade and Industry (2005) *Science budget allocations: 2005-06 to 2007-08*, available at: http://www.bis.gov.uk/files/file14994.pdf, p6.
[488] Department for Business, Innovation and Skills (2012) *SET statistics - science, engineering and technology indicators*, available at: http://www.bis.gov.uk/assets/biscore/science/docs/s/12-499-set-statistics-2012.xls, Table A3.1.
[489] Ibid, Table A3.2.
[490] Ibid.
[491] One of the five 'headline targets' for measuring progress in meeting the goals of the Europe 2020 growth strategy for the EU and, conspicuously, the only input target (the other four being outcome targets) is for three per cent of the EU's GDP (public and private combined) to be invested in R&D/innovation; "…more R&D/innovation in the economy, combined with more efficient resources, makes us more competitive and creates jobs". European Commission (2011) *Europe 2020 targets*, available at: http://ec.europa.eu/europe2020/targets/eu-targets/index_en.htm.
[492] See: http://www.innovateuk.org. The TSB further describes itself, aims and methods: "…the UK's national innovation agency. Our goal is to accelerate economic growth by stimulating and supporting business-led innovation. We understand business, and our people come mainly from business. We work right across government, business and the research community - removing the barriers to innovation, bringing organisations together to focus on opportunities, and investing in the development of new technology-based products and services for future markets." Technology Strategy Board (2011) *Concept to commercialisation: a strategy for business innovation, 2011-2015*, available at: http://www.innovateuk.org/_assets/0511/technology_strategy_board_concept_to_commercialisation.pdf, p2.
[493] For example: "… Government can be an important driver of innovation. We will support independent bodies, like the Technology Strategy Board, to intervene when the market is unable to foster innovation alone in critical technologies or sectors." Department for Business, Innovation and Skills (2011) *Innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/i/11-1387-innovation-and-research-strategy-for-growth.pdf, pV.

overall rationale is confirmed in the 2010 allocation document that lays out the science settlement:

> "Research Councils and Funding Councils will be able to focus their contribution on *promoting impact through excellent research, supporting the growth agenda*. They will provide strong incentives and rewards for universities to improve further their relationships with business and deliver even more impact in relation to the economy and society."[494]

7.13 Apparent from successive policy documents stretching back before the 2010 general election is a movement towards the Government choosing very particular areas of research to focus on and doing so in consultation with the private sector.[495] This is what would be expected given the focus (however unrealistic) on research policy geared towards innovation in the private sector. However, it is noteworthy how the framing of such decisions have become progressively more narrowed to the economic dimension, almost to the exclusion of other considerations. Combined with this narrowing of the decision frame around economic criteria is a conviction that the expected outcomes can be achieved through a suitable alignment of favourable conditions. This is epitomised by the extension of technology 'roadmaps' to the life sciences supported by 'leadership councils' comprising academics, industrialists and research councils.[496] For example, a synthetic biology roadmap, published in August 2012, contains recommendations to "provide a compass-bearing for the synthetic biology community, helping to align interests towards future growth opportunities…"[497]

7.14 Synthetic biology was selected as an area to which support should be given, according to the Department of Business, Innovation and Skills' document *Innovation and research strategy for growth*, on the basis of a 'robust analytical framework', drawing on expertise in business, the TSB, the research councils, public sector research establishments, universities, and infrastructural organisations. This was used to evaluate technologies against a number of key criteria:

- the potential size of the global market, and its rate of growth;
- the range of applications for the technology across a number of economic sectors;
- the capability of the research base to develop these technologies (number of published papers, active research projects);
- number and strength of UK firms and their supply chains relative to international competitors, and their ability to adopt and exploit the technologies; and

[494] Department for Business, Innovation and Skills (2010) *The allocation of research science funding, 2011/12 to 2014/15: investing in world-class science and research*, available at: http://www.bis.gov.uk/assets/biscore/science/docs/a/10-1356-allocation-of-science-and-research-funding-2011-2015.pdf, p5. (Emphasis in original).

[495] The documents to which we refer include: Department for Business, Innovation and Skills (2011) *A vision for UK research* available at: http://www.bis.gov.uk/assets/cst/docs/files/whats-new/10-584-vision-uk-research; Department for Business, Innovation and Skills (2011) *Innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/i/11-1387-innovation-and-research-strategy-for-growth.pdf; Department for Business, Innovation and Skills (2010) *Technology and innovation futures: UK growth opportunities for the 2020s* available at: http://www.bis.gov.uk/assets/foresight/docs/general-publications/10-1252-technology-and-innovation-futures.pdf (in which 53 specific future technologies and innovations were identified. See p25ff).

[496] For example, the synthetic biology 'leadership council' is co-chaired by the Minister and a senior industry figure, with the roadmap group chaired by the industry co-chair of the Council. See: House of Lords Hansard (6 December 2011) *c695*, available at: http://www.publications.parliament.uk/pa/ld201011/ldhansrd/text/111206-0002.htm.

[497] Research Councils UK (13 July 2012) *Research roadmap paves the way for UK synthetic biology*, available at: http://www.rcuk.ac.uk/media/news/2012news/Pages/120713.aspx. See also paragraph 6.33ff.

- ability to capture and protect the value we create (patenting, embedding and exploiting intellectual property).[498]

7.15 Synthetic biology was chosen as an area which should be supported because "[e]stimates put the world market at around $100 billion by 2020. The UK produced 14 per cent of all global research papers between 2005 and 2010. The potential applications include bacteria that feed on pollutants, new biofuels, drought and disease resistant crops. The UK has leading companies in these sectors."[499] The *Strategy for UK life sciences,* published around the same time, similarly notes that synthetic biology "was recently identified by the TSB as a key emerging technology with the potential to create a billion pound industry within the UK in the next decade."[500]

7.16 The *Strategy for UK life sciences* in fact corrals the whole area of medical research (on which it is almost exclusively focused) into the guiding objective of generating economic benefit. The essential assumptions behind the Strategy appear to be that the life science industry is large and fast growing, and, in particular, that the UK has a strong record of life sciences research. The fact that the contribution of the life sciences industry to growth does not match this record is explained by the further assumption that the realisation of this potential growth is held back by problems in clinical research, translation, and a failure to exploit the potential of the National Health Service.[501] Similar arguments underlie the recent MRC, BBSRC, Engineering and Physical Sciences Research Council (EPSRC), Economic and Social Research Council and TSB document *A strategy for UK regenerative medicine*.[502]

7.17 It is worth stressing that the discussion of impact in these documents, extensive as it is, is of expected and hoped-for impact, rather than of impact of past research. Indeed a striking feature of research policy documents is the lack of assessment of previous cases, conspicuous given that there has been at least 30 years of emphasis on the economic exploitability of academic research, and of large scale support for commercialisation.

Charities

7.18 Before discussing the assumptions that appear to underlie current research policy, we should note the contribution of medical charities, which fund very substantial amounts of research in the UK. Three bodies dominate funding: in order of expenditure these are the Wellcome Trust, Cancer Research UK and the British Heart Foundation.[503] In these cases, and indeed most

---

[498] Department for Business, Innovation and Skills (2011) *Innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/i/11-1387-innovation-and-research-strategy-for-growth.pdf, pp28-9.

[499] Ibid, p29.

[500] Department for Business, Innovation and Skills (2011) *Strategy for UK life sciences*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences, p10.

[501] Ibid.

[502] Medical Research Council (2012) *A strategy for UK regenerative medicine*, available at: http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC008534. It is claimed in this document that "Regenerative medicine is an emerging discipline that holds the promise of revolutionising patient care in the 21st Century", that the "UK is a leading player globally in the science that underpins regenerative medicine", and that, currently, "the UK is at the forefront of this rapidly evolving field" (p2). The document, however, is essentially a report on current funding arrangements mostly for 'underpinning' (i.e. basic) research in this area. It is not, in fact, clear that regenerative medicine can be treated homogeneously as an 'emerging discipline' because it embraces too heterogeneous a group of technologies (gene therapy, stem cell grafts, tissue engineering etc.).

[503] In 2011, the Wellcome Trust Group spent £641.8 million on charitable activities (£392.6 million on 'science funding', £117.3 million on the Wellcome Trust Genome Campus, £74.7 million on 'technology transfer' and £57.2 million on 'medical humanities and engagement'); Cancer Research UK spent £340.4 million on charitable activities (£324.7 million on 'research' and £15.7 million on 'information and influencing public policy'); the British Heart Foundation spent £310.3 million on charitable activities (£120.7 million on 'research funding', £34.5 million on 'prevention and care' and £155.1 million on 'expenditure in furtherance of charitable objectives'). In 2010/11, the MRC spent £264.4 million on research grants and £25.9 million on 'other research' (which largely relates to joint funding and strategic partnerships). See: Wellcome Trust (2011) *Annual report 2011*, available at: http://www.wellcome.ac.uk/stellent/groups/corporatesite/@msh_publishing_group/documents/web_document/wtvm053879.pdf, p45;Cancer Research UK (2012) *Beating cancer, saving lives: our annual report and accounts, 2011/12*, available at: http://www.cancerresearchuk.org/prod_consump/groups/cr_common/@abt/@gen/documents/generalcontent/cr_088965.pdf, p23; British Heart Foundation (2011) *Where your money goes: annual review 2011*, available at: http://www.bhf.org.uk/publications/view-publication.aspx?ps=1001757 and Medical Research Council (2012) *Annual report and accounts 2010/11*, available at: http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC008586, p106.

other instances where charities fund research, the aim of research is to have an impact consistent with the charitable aims of the organisation in question, for example the improvement of public health, rather than the improvement in profit margins in the pharmaceutical industry or indeed improvements to the UK economy itself.[504] The documents we reviewed (strategic plans, grant writing guides etc.) also reflected the difficulty of properly assessing non-economic impact: there was little in the way of explanation as to how such impact could be properly quantified and measured, although the Wellcome Trust has produced an 'assessment framework' ("established to enable progress to be tracked against… ten key indicators of progress…"[505]).This attempts to capture both quantitative and qualitative information with regard to the impact and outcome of Wellcome Trust funded research.[506] However, such documents are retrospective in nature and understandably offer little in the way of a framework for *predicting* impact on this basis of past work. Other documents reviewed that dealt with issues relating to funding decisions noted considerations such as "tangible impacts on health" and "discernable impact on wider policy development and practice";[507] novelty and relevance;[508] and, "relevance to cardiovascular disease, scientific merit, [and] timeliness".[509]

7.19 Published sources provide little guidance on how charities identify research priorities, although the main three medical charities all stress scientific excellence and impact on human health as key criteria. As with Government policies, there appears to be no special role granted to the concept of emerging biotechnologies within the published policy documents of those charities.

Framing research policy

7.20 In view of the history of commercialisation in the life sciences, there is a dilemma for policy that is orientated by expectations of substantial national economic benefit: if past evidence is irrelevant to newly emerging biotechnologies then it provides no basis for the expectation; if the evidence is relevant then the expectation is likely to be misplaced.[510] Understanding this dilemma involves examining the commonplaces and assumptions that frame the dominant policy discussions. This is, of course, not to explain these claims fully (since it merely begs the question of how those commonplaces came about in the first place), but to draw attention to the lack of explicit reflection on this on the part of those who assert them. In this section we therefore discuss the background assumptions in the documents to which we have already referred. Specifically, we look critically at the framing of choices through which important conditions, namely funding of different technology trajectories, are set.

---

[504] In a review of some of the five largest (by expenditure on medical research) charitable funders' policy documents we found that only Arthritis Research UK explicitly mentions 'economic' impact as a specific goal, stating that it aims to "[r]educe the economic impact of arthritis on the individual patient, their family and the wider economy". See: Arthritis UK (2012) *Annual report and financial statements 2010-11*, available at: http://www.arthritisresearchuk.org/about-us/~/media/Files/Annual-Review-and-Reports/12570-Report%20-Accounts-2010-11.ashx, p5.

[505] The Wellcome Trust (2011) *Assessment framework report 2010/11*, available at: http://www.wellcome.ac.uk/About-us/Publications/Reports/Biomedical-science/WTVM054494.htm.

[506] See: Wellcome Trust (2012) *Assessment framework report: report summary 2010/11*, available at: http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/WTVM054488.pdf.

[507] Wellcome Trust (2005) *Strategic plan 2005-2010: making a difference*, available at: http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/wtd018878.pdf, p27.

[508] Cancer Research UK (2006) *Grant writing guide*, available at: http://www.cancerresearchuk.org/science/prod_consump/groups/cr_common/@fre/@fun/documents/generalcontent/grant-writing-guide.pdf, p1.

[509] British Heart Foundation (2012) *How we fund*, available at: https://www.bhf.org.uk/research/research-grants-1/how-we-award.aspx.

[510] Part of this explanation may lie in understanding the 'productivity paradox' that has puzzled economists, which was summed up (in relation to computer technology) in the observation that "we see the computer age everywhere except in the productivity statistics." (Brynjolfsson E and Hitt LM (1998) Beyond the productivity paradox *Communications of the ACM* **41**: 49-55, citing Robert Solow. While this may point only to the unanticipated length of time by which productivity benefits lag behind technological diffusion owing to the costs and complexities of innovating (i.e. the benefits will show up *eventually*), the paradox relates to technologies that have already been developed and diffused. Development and innovation are formidable hurdles that still lie ahead when one is speaking of emerging biotechnologies.

7.21 Although stronger assumptions are made in many policy documents, the following beliefs are generally found together in some form or other as a background against which policy decisions are made:

- the UK 'science base' in the life sciences is exceptionally strong in international comparisons;
- the UK pharmaceutical industry – the research-intensive (non-generic) part – is a high-tech, high value-added industry that makes it economically extremely valuable to the UK;
- there is a causal connection between (a) and (b) in that the research base powers the success of the industry, and that the success of the industry ensures the applicability of research in the UK;
- biotechnology is becoming more and more important to the pharmaceutical industry (as well as some other industries where UK is less strong);
- some areas of the underlying science have 'cross-over potential', notably synthetic biology, so they might help to give the UK 'lift-off' in chemical and agricultural biotechnology; and
- public spending on research is, in many cases, justifiable only where there is potential to generate economic growth in the UK.

7.22 These assumptions are often surprisingly resistant to evidence. Particular ways of thinking, for example, about transformative technologies, about the nature of UK research and about its relationship to the UK economy, are prevalent in policy discussion without being subjected to scrutiny concerning either their foundation or their contemporary relevance. This is, in part at least, because policy makers operate within a detached world that is subject to dominant frames where, in this as in other areas, policy objectives shape the search for and interpretation of evidence, and where interested parties create influential narratives to which public policy responds.[511] It is an example of a phenomenon that we identified in Chapter 2, whereby the self-reinforcing nature of the discourse displaces ambiguous or even inconvenient evidence that challenges the integrity of the established frame as a foundation for judgment. The dynamic is similar to that that we observe creating the 'biotech boom' in Chapter 9.

'Britain is good at research and invention but bad at commercialisation'

Research and commercialisation of technologies generally

7.23 The idea that the UK is peculiarly good at inventing and/or scientific research is an important element in many arguments in research policy and, indeed, in the national self-image. This claim has become particularly focused on life sciences research and, in this area, is accompanied by the claim that the UK is also good at application but remains hampered by important barriers to commercialisation. This assumption would therefore give grounds for optimism and investment in biosciences and especially in commercialisation if the obstacles to commercialisation could be identified and addressed. The associated rhetoric is suggestive of notions of 'unlocking potential'.

7.24 The claim is conventionally grounded on evidence of comparatively high publication and citation rates for UK research. The obstacles to commercialisation are associated with terms like the 'valley of death' (that separates basic biomedical research from clinical application) and questions about the lack of a UK success story of the scale of Google or Apple. This supports a policy focus on innovation to unlock assumed economic potential.

[511] See: Orlikowski WJ (2000) Using technology and constituting structures: a practice lens for studying technology in organizations *Organization Science* **11**: 404-28.

7.25 The two-part 'good at research, bad at commercialisation' argument has been a standard theme in discussion of UK research for well over a century. It is well established that the UK has been one of a small number of countries that have been notable for invention and research, and these few countries have long dominated research. However, this does not mean that the UK has been or is radically better than its main competitors in research, or indeed 'the best'. If we believe that the UK is in competition with other states over innovation, we should consider the position of the UK in relation to its peers as innovators, competing for the benefits to be had from innovation, rather than in relation to all countries, since other countries may have chosen to be 'innovation takers' (i.e. not investing in their own R&D).

7.26 The second part of the two-part claim – the idea that the UK has failed to develop research findings and inventions – is contradicted by much of its recent history. Until the 1970s, for example, development expenditure by both Government and industry was relatively high (except by comparison with the US). Furthermore, many new technologies were brought to market in the UK, including jet engines, nuclear power stations and pharmaceuticals. Of course, successful initial commercialisation does not necessarily mean economic success, but it would be hard to maintain that the UK Government or industry were ineffective, before the 1970s at least, in supporting emerging technologies and bringing them to market. Furthermore, the UK had a very good record of developing and using techniques pioneered elsewhere.[512]

7.27 While there may be no general cultural or historical basis for the two-part claim it may, nevertheless, be the case that the claim applies now. Across the board, in academic research, the UK fares comparatively well.[513] However, the publication and citation measures now commonly used to calculate this offer no reliable proxy for innovation. Neither do patent counts, where the UK's percentage of world patenting is well below Germany and just below France.[514] By a wider measure, including patents and R&D expenditures, the Organisation for Economic Co-operation and Development (OECD) does not currently place the UK as an innovation leader, but as an 'innovation follower'.[515] As far as commercialisation is concerned, industrial R&D is a key factor and this is clearly lower in the UK as a proportion of GDP that in countries such as the US, Germany, Japan, and the Republic of Korea, among others. To that extent the UK is no longer 'good' at industrial development in general.

Research and commercialisation in the biosciences

7.28 So, is the UK 'good at research' in the biosciences? Contemporary claims for UK research superiority generally draw specifically from the life sciences, and some analyses of citations bear this out.[516] Other figures put the UK performance, though strong in a global context, in a slightly more modest light.[517] What all the figures show, however, is that the UK generates a

[512] Such as the electronic television.

[513] The UK accounts for roughly one per cent of the world population and 11.9 per cent of citations (Vaitilingam R (2010) *Research for our future: UK business success through public investment in research*, available at: http://www.rcuk.ac.uk/documents/publications/researchforourfuture.pdf, p5). Clearly, the UK does better than the world average, but this is only to be expected. We also need to compare with key competitors such as the US, Germany, and France. The UK does do better than these countries (other than the US), but the differences are not huge. For example, field-weighted citations between 2006 and 2010 were around 1.42, compared with about 1.2 for Italy, with Canada, Germany and France in between. (Elsevier (2011) *International comparative performance of the UK research base - 2011*, available at: http://www.bis.gov.uk/assets/biscore/science/docs/i/11-p123-international-comparative-performance-uk-research-base-2011, p36, figure 4.7).

[514] Ibid, figure 7.1.

[515] Department for Business, Innovation and Skills (2011) *BIS economics paper no.15: innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/BISCore/innovation/docs/E/11-1386-economics-innovation-and-research-strategy-for-growth.pdf, pp39-49.

[516] The Department for Business, Innovation and Skills, for example, reports that UK publications in bioscience from 2006-2009 received an average of 9.5 citations each, higher than any other country. Department for Business, Innovation and Skills (2011) *Strategy for UK life sciences*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences, p12.

[517] For all countries the two big categories in terms of total numbers of papers are clinical sciences and biological sciences. (Health and medical sciences is much smaller, so we this for present purposes.) Elsevier (2011) *International comparative performance of the UK research base - 2011: appendix F: supplementary data*, available at: http://www.bis.gov.uk/assets/BISCore/science/docs/l/11-p123an2-international-comparative-performance-uk-research-base-

great number of research papers (both by absolute and *per capita* measures), and that the best of these compare favourably with the best in the world (in terms of citation impact). However, there are also a great number of papers produced in the UK that do not measure up in these terms (a slippage down the rankings in terms of citations per paper) with field weighted citation impact ranking of 12th in the OECD for clinical sciences and fourth for biological sciences. However, it is not the case that these are areas in which the quality of UK output is relatively higher compared to other areas of research.[518] So UK research in biosciences is strong, but not exceptional compared to other countries and UK biosciences research is not exceptionally strong compared to other areas of research.

7.29 The second question to address is whether the UK is 'bad at commercialisation' in the biosciences? It is claimed that UK research in the biosciences has given rise to successful domestic commercialisation, such as to give confidence in the promise of future biotechnologies, with the pharmaceutical industry providing the guiding example that policy would like to follow and repeat in other areas. Figures that are widely available, however, give no evidence as to where the relevant research or development was carried out; they tell us only that firms with headquarters in the UK were quite successful in developing and selling drugs.[519] While this evidence therefore points to the fact that there is successful and profitable commercialisation by UK-headquartered firms, there is no such evidence that supports the suggestion that research carried out in the UK is similarly successful.

The safety of the assumption

7.30 In summary, there is little evidence to link the relatively strong underpinning research carried out in UK institutions with successful commercialisation of underpinning research by UK firms, despite the frequency of claims to this effect. In any case, as we have argued above,[520] historical experience of other fields – particularly in the physical and information sciences – may not be a reliable guide in the field of biotechnologies. Furthermore, the experience of domestic commercialisation in biotechnology, chiefly drawn from the pharmaceutical industry may not be a reliable precedent for other areas of biotechnology and, in any case, is relatively unremarkable (in terms of the specifically biotech component).

7.31 There are a number of conclusions that we can draw from the foregoing considerations that recommend caution and further reflection on the basis for UK policy in the life sciences. These relate to the features of emerging biotechnologies that we identified in Chapter 3. It is not clear that the UK's life sciences academic research sector is unusually productive, nor is it clear that

---

2011-f.pdf provides useful information on article and citation shares. For clinical science, in 2010 the UK world article share was 8.0%, second to US with several countries between 8% and 4% (p38). The UK citation share was 12.5%, in second place behind the US but ahead of Germany, which had around 9% (p60); the UK had 16% of the most highly cited papers (p93). However, for citations per article the UK was 11th in the OECD (p71); field weighted citation impact 12th in OECD (p82). For biological sciences, in 2010 the UK had 6.9% of articles, in third place behind the US and China but level with Japan and Germany, and 11% of the citation share, ahead of Germany at 9% (p62); within this, the UK had 14.5% of highly cited (p95). But citations per article were 4th in the OECD (p73); the field weighted citation impact 4th in OECD (p84).

[518] "UK research quality is high across all subject fields. The UK's field-weighted citation impact is especially strong in fields where it has relatively lower publishing activity – especially mathematics, physical sciences and engineering". Elsevier (2011) *International comparative performance of the UK research base - 2011*, available at: http://www.bis.gov.uk/assets/biscore/science/docs/i/11-p123-international-comparative-performance-uk-research-base-2011, p39.

[519] For example, it is claimed that "around one fifth of the world's top 100 medicines originate from UK research." (House of Commons Hansard (21 March 2012) *c799*, available at: http://www.publications.parliament.uk/pa/cm201212/cmhansrd/cm120321/debtext/120321-0001.htm.) The basis for this claim might be that 20% of the top 75 drugs by global sales were originated by firms whose headquarters were in Britain. (IMS/ABPI calculations Pharmaceutical Industry Competitiveness Task Force (2009) *Ministerial Industry Strategy Group, Pharmaceutical Industry: competitiveness and performance indicators 2009* available at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_113133.pdf, p26.) Another statistic suggests that medicines originating from UK firms captured a 16% value share of the world's 100 top selling drugs in 2008 (ABPI, cited in UK Department for Business, Innovation and Skills (2011) *Strategy for UK life sciences*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences, p25.). British firms' market share for products launched in the five years up to 2009 was 11%, 9th in the world (Association of the British Pharmaceutical Industry (2012) *Global pharmaceutical industry and market*, available at: http://www.abpi.org.uk/industry-info/knowledge-hub/global-industry/Pages/industry-market-.aspx, figure 3).

[520] See Chapter 6.

this could transmute into a successful life sciences industry, not least because a strong pharmaceutical industry is not necessarily evidence of capacity to create new drugs. Furthermore, it is not clear that the business-focused policy, even if successful, would be the most effective in addressing problems of human health and welfare, in the UK or elsewhere. Government has, from the point of view of the growth agenda, sought to find areas where UK basic research is strong, and where there is a relatively strong industrial base, and in this case the life sciences sector appears to have particular promise, if it is the case that research advances can be captured in the UK. However, even though there is no obvious linked industrial sector, relative strength may be greater in other sectors of basic research. Furthermore, there are weaknesses in industrial areas where one might expect and hope for major developments in emerging biotechnologies, such as industrial biotechnology.[521]

7.32 To draw these conclusions is not to say that the policy focus on life sciences is misplaced, but rather that it is at least not as well-founded as it is often made to appear. This could be equally true, of course, of many alternative policies that are focused on emerging biotechnologies. These conclusions do not counsel against ambitious policy but call for candour, public reasoning and caution. Certainly there is a need for evidence-based policy in this area, but this does not merely mean an extension of currently used forms of quantitative evidence. There is a tendency to consider quantitative evidence as superior because it is more manageable, which has led to unhelpful, and occasionally absurd, attempts assess a greater range of impacts in quantifiable, and especially economic, terms. Rather than the attempt at reductionism of this sort to make relevant evidence manageable within an existing decision frame, **the determination of biotechnology policy should attend explicitly to diverse perspectives and bodies of evidence rather than privileging a single, quantitative frame of evaluation (such as economic costs and benefits, or costs and benefits reduced to economic values)**; this should be the case not only at the 'macro' level of Government policy but also at the 'meso' level of funding bodies and, indeed, at the 'micro' level of research (as we discussed in Chapter 6). This would encourage a more critical consideration of the interests that research may promote and, in particular, how it might promote the public good (and how this good is construed) rather than merely economic growth or wealth creation.

Scientific knowledge as a public good

7.33 The standard justification for state-funded research arises from a particular analysis of scientific knowledge being a 'public good' in the sense that this is understood by economists, namely, that it will not be adequately provided by markets, and that it is nevertheless desirable because it furthers the ends of society. (We discuss how the degree to which biotechnologies may be thought of as public goods in Chapter 4.) If scientific knowledge were a 'public good' in the sense of being 'non-excludable' it would be hard to explain state funding of research in a competitive multi-state world. Indeed, in such a world, the argument would be that states would, and should, *under*-invest in research. On this model, the deficit could only be made up by a world-state, not a national state.[522]

[521] See, generally, Skibar W, Grogan G, Pitts M and Higson A (2009) *Analysis of the UK capabilities in industrial biotechnology in relation to the rest of the world – follow-up report to: assessment of current activity in the production of platform chemicals from renewable sources and horizon scan to forecast potential future developments in science and technology activity in biocatalysis*, available at: http://www.bis.gov.uk/files/file51237.pdf; Industrial Biotechnology Innovation and Growth Team (2009) *IB 2025 maximising UK opportunities from industrial biotechnology in a low carbon economy: a report to government by the Industrial Biotechnology Innovation and Growth Team* available at: http://beaconwales.org/uploads/resources/Maximising_UK_Opportunities_from_Industrial_Biotechnology_in_a_Low_Carbon_Economy.pdf.

[522] For a discussion of the economics of scientific and technical research, see: Nelson RR (1959) The simple economics of basic scientific research *Journal of Political Economy* **67**: 279-306; Hounshell DA (2000) The medium is the message, or how context matters: The RAND Corporation builds on economics of innovation, 1946-1962, in *Systems, experts, and computers: the systems approach in management and engineering, World War II and after* Hughes AC, and Hughes TP (Editors) (Cambridge, Massachusetts: MIT Press) Pestre D (2003) *Science, argent et politique: un essai d'interprétation* (Versailles: Quae); Arrow KJ (2011) Economic welfare and the allocation of resources for invention, in *The rate and direction*

7.34 In reality, much scientific knowledge does not meet the criteria of being a public good in this classic, economic sense. Scientific knowledge is, in fact, excludable to a large extent, through secrecy, patenting, or high costs of access.[523] The actual reasons states fund research are not self-evident, but are likely to be neither simply an acceptance of market failure nor a universal philanthropy. They may include, for example, military security and national economic growth. On the other hand, many things that states do, such as providing overseas aid, are not easily analysable in terms of a simple rule, such as to maximise gross national product, but recognise instead the complex interdependencies and trade-offs, on a number of different levels, of belonging to a global community. Even a ruthlessly competitive state may recognise advantages to cooperation or the expediency of developing overseas markets.

7.35 Among the ways in which the public good might be promoted by publicly funded research is through the creation of public knowledge available to all, created independently of private interests. In general, there might be a case for ensuring that the public and those acting in its interest have the countervailing knowledge required to assess private, interested claims for example, claims for the efficacy of particular drugs.[524] This would also entail active support for independent research, recognising as a central issue, that not all – indeed, not much – research will be independent.[525] Such public knowledge should contribute to a new and more explicit appreciation of the limits of knowledge and prediction in the face of uncertainties, with the aim of bringing an end to over-promising.

National research and economic growth

7.36 Innovation, derived to a significant degree from research and development, has transformed the world and has permitted large increases in both varieties and levels of output. The relationship between national R&D investments and national rates of economic growth is, obviously, highly dependent on particular circumstances, but it cannot be assumed that national R&D expenditures are a major determinant of national growth rates. The extent of the relationship will vary by country and with time, as well as with policy: what might hold for the US, or Japan, or the world as a whole, will not necessarily hold for any particular country.

7.37 Nevertheless, the assumption is made that national research is critical to national growth, and that if it does not lead to growth there must be a problem of translation, development funding, or investment. This is not necessarily so, however: most countries get most of their innovations from abroad (though it is worth noting that in some cases this might involve national R&D). The assumption that, as far as research is concerned, nations are economic and scientific units competing with each other, and that research is one of the most powerful weapons in that economic contest may well be mistaken. Nations are not generally competing with each other, something like free trade operates between nations, and research activity is only partially organised nationally.

7.38 In fact it might be quite misleading to identify R&D performed in a particular nation with that nation. Excluding defence and related R&D which is clearly national, most private research is concerned with the growth of particular firms, not the nation in which they contingently operate. Indeed in the UK, approximately 22 per cent of business R&D is funded from abroad (considerably higher than for other countries),[526] and the proportion of R&D carried out by

of inventive activity: economic and social factors, Groves HM (Editor) (Princeton, New Jersey: Princeton University Press)
Mirowski P (2011) *Science-mart: privatizing American science* (Cambridge, Massachusetts: Harvard University Press).

523 We discuss the commercial exploitation of such knowledge in Chapter 9.

524 See: Angell M (2005) *The truth about the drug companies: how they deceive us and what to do about it* (New York: Random House); Borch-Jacobsen M (2010) Which came first, the condition or the drug? *The London Review of Books* 7 October, available at: http://www.lrb.co.uk/v32/n19/mikkel-borch-jacobsen/which-came-first-the-condition-or-the-drug; Agnell M (2011) The illusions of psychiatry *The New York Review of Books* 14 July, available at: http://www.nybooks.com/articles/archives/2011/jul/14/illusions-of-psychiatry/?pagination=false.

525 See, for example, Goldacre B (2012) *Bad pharma: how drug companies mislead doctors and harm patients* (London: Fourth Estate).

526 Department for Business, Innovation and Skills (2011) *BIS economics paper no.15: innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/BISCore/innovation/docs/E/11-1386-economics-innovation-and-research-strategy-for-growth.pdf, p47.

foreign multinationals within the UK is much higher than this, at around 40 per cent.[527] Much of the remaining 60 per cent is performed by UK-based multinationals whose operations and success are not necessarily tied to that of the UK economy. The pharmaceutical industry reproduces these proportions.[528] At best then, only a fraction of R&D contributes to national growth, and the location of activities within a particular national boundary does not mean that they are part of a system working for national purposes. Nevertheless, it seems that, rhetorically at least, much research council funding is directed to increasing the rate of economic growth of the UK through both research output and the output of people trained in advanced scientific methods, who enable the economy to assimilate and exploit new knowledge, whether that arises from research in the UK or elsewhere.

7.39 Thus the proposal that the output of research could be the basis of billion pound UK industries within a few years is highly uncertain, not to say unlikely. Even taken more broadly, the argument in favour of strategic investment in research in particular areas needs to be made extremely carefully. Such arguments cannot be founded uncritically on the assumption that a straightforward and strong positive correlation between investment in research and national growth can be expected.

7.40 This might lead us to question the plausibility of the expectation that synthetic biology will create a business worth $100 billion by 2020[529] and that UK firms, or firms in based in the UK, will take a significant share (say 10%). Our reflections may be coloured by the recognition that, in recent years, apparently grossly inflated estimates for the value of nanotechnology industry were made, for example that the industry would be worth $1 trillion by 2016.[530] If this were considered to be a distinct possibility, then a question could be raised as to why private firms would not fund synthetic biology research entirely themselves. Or, the problem may be that, in the case of emerging biotechnology, the venture capital model for funding might not work as it has for information and communications technology.[531] If this is thought to be the problem, then major interventions and subsidies – more radical than those of the 1970s – would be needed, yet they are clearly not on the political agenda. Furthermore, we should recognise that if we were to have $100 billion industry by 2020, the research, and most of the development, would already have to have been done.

7.41 After 30 years of focus on biotechnology, the modesty of UK success stories in the policy literature is striking.[532] All of this seems to confirm a dissonance between the promissory rhetoric and the material uncertainties, of the sort that we identified in Chapter 2, which has led to policy based on the elements of the discursive frame – such as the assumptions we discuss here – rather than a reflection on how the uncertainties and complexities of the innovation process in respect of emerging biotechnologies specifically challenge this frame.

The centrality of biotechnology to a transformed future

7.42 It has been suggested that biotechnology will be central to a coming wave of social and economic transformation among those looking for a worthy successor to the information

[527] Ibid, p48.
[528] Sixty per cent of total R&D investment in the UK pharmaceutical sector was carried out by UK-owned firms in 2008 (see: Department of Business, Innovation and Skills (2010) *BIS economics paper no.2: life sciences in the UK – economic analysis and evidence for 'life sciences 2010: delivering the blueprint'*, available at: http://www.bis.gov.uk/assets/biscore/economics-and-statistics/docs/10-541-bis-economics-paper-02, pViii).
[529] Department for Business, Innovation and Skills (2011) *Innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/i/11-1387-innovation-and-research-strategy-for-growth.pdf, p29.
[530] Roco MC and Bainbridge W (2001) *Societal implications of nanoscience and nanotechnology*, available at: http://www.wtec.org/loyola/nano/NSET.Societal.Implications/nanosi.pdf, p3.
[531] For limitations of the venture capital model see: Browning J (2009) The incredible shrinking venture capital *Nature* **460**: 459.
[532] See the policy documents cited elsewhere in this Report (e.g. in paragraphs 7.12ff). See also: The Royal Society (2010) *The scientific century: securing our future prosperity*, available at: http://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/publications/2010/4294970126.pdf.

revolution of the late 20th Century.[533] For example, the BBSRC's 2011-15 delivery plan, begins by asserting that "the 21st Century will be the age of bioscience." It continues:

> "Driven by new concepts and technologies, a biological revolution is unfolding in the same way that advances in physics shaped the early 20th Century and great leaps in electronics and computing transformed our lives over the past 40 years.
>
> Modern bioscience offers *enormous benefits to society and unprecedented opportunities for innovation and growth in multi-billion pound sectors of our economy* such as food and drink, agriculture, biotechnology, energy, health and pharmaceuticals."[534]

7.43 Claims such as these can come to stand as justification for the idea that the UK should be strong in these sectors and, indeed, that by not committing to them it would miss vital opportunities. We need to be wary of the assumption that high technology industries are all fast growing, that they are fast growing everywhere and that such industries are necessarily major drivers of economic growth. In the UK between 1992 and 2007 the contribution of high and medium technology sectors to the total growth in economic output was approximately five per cent, compared with approximately 20 per cent for Germany and 40 per cent for Japan and the Republic of Korea.[535] The pharmaceutical industry may, globally, be growing faster than the world economy, but its growth rate is far from exceptional, and there is no guarantee or evidence that pharmaceutical firms based in the UK with a high R&D-intensity will grow significantly faster than the world economy, or even the UK economy as a whole.[536]

Directing technologies and supporting diversity in research

7.44 A more critical approach is needed in response to the assumption that pharmaceuticals and biotechnology have been (or are) radically promising sectors from the point of view of economic benefit. In fact the most obvious and salient point about the pharmaceutical industry is that it has seen a significant *fall* in the productivity of R&D. Indeed, although the medical biotechnology sector has been subject to massive investments over 30 years, there has been relatively little return to date. There is also evidence on the supposed biotechnological revolution that suggests, at the very least, that claims for future biotechnology-led transformations should be treated with some scepticism.[537] Moreover, it would be a great mistake to equate improvements to human health *necessarily* with expenditures on pharmaceuticals, or the growth, productivity or profitability of the industry, as a large critical literature on the industry makes clear.[538] The case of pharmaceuticals may be a conspicuous case of what some analysts take to be a more general phenomenon, namely the possible

---

[533] See: Freeman C (1992) *The economics of hope: essays on technical change, economic growth and the environment* (London: Pinter).

[534] BBSRC (2011) *BBSRC delivery plan 2011-2015: maximising economic growth in the age of bioscience*, available at: http://www.bbsrc.ac.uk/web/FILES/Publications/delivery_plan_2011_2015.pdf, p3, emphasis in original.

[535] Department for Business, Innovation and Skills (2011) *BIS economics paper no.15: innovation and research strategy for growth*, available at: http://www.bis.gov.uk/assets/BISCore/innovation/docs/E/11-1386-economics-innovation-and-research-strategy-for-growth.pdf, p33. See also: OECD (2012) *STAN database for structural analysis*, available at: http://stats.oecd.org/Index.aspx?DatasetCode=STAN08BIS.

[536] IMS Health (amongst other roles, an information provider for health care industries), reported that the total global pharmaceutical market grew 6.2 per cent annually for five years until 2011. Global GDP growth was 5.3 per cent in 2010 and 3.9 per cent in 2011. See: IMS Health (18 May 2011) *IMS Institute forecasts global spending on medicines to reach nearly $1.1 trillion by 2015*, available at: http://www.imshealth.com/portal/site/ims/menuitem.d248e29c86589c9c30e81c033208c22a/?vgnextoid=01146b46f9aff210VgnVCM100000ed152ca2RCRD&vgnextchannel=4eb65890d33ee210VgnVCM10000071812ca2RCRD&vgnextfmt=default and International Monetary Fund (2012) *World economic outlook April 2012: growth resuming, dangers remain*, available at: http://www.imf.org/external/pubs/ft/weo/2012/01/pdf/text.pdf, p2.

[537] Hopkins MM, Martin PA, Nightingale P, Kraft A and Mahdi S (2007) The myth of the biotech revolution: an assessment of technological, clinical and organisational change *Research Policy* **36**: 566-89.

[538] For example: Angell M (2005) *The truth about the drug companies: how they deceive us and what to do about it* (New York: Random House); Agnell M (2011) The illusions of psychiatry *The New York Review of Books* 14 July, available at: http://www.nybooks.com/articles/archives/2011/jul/14/illusions-of-psychiatry/?pagination=false; Le Fanu J (2011) *The rise and fall of modern medicine* (London: Abacus); Mirowski P (2011) *Science-mart: privatizing American science* (Cambridge, Massachusetts: Harvard University Press). See, also: Goldacre B (2012) *Bad pharma: how drug companies mislead doctors and harm patients* (London: Fourth Estate).

slowing of innovation in recent decades. Such a conclusion stands in sharp contrast to the repeated assertion that we are living in an age of unprecedented innovation.[539]

7.45 We conclude that a belief about what technologies will be of central importance, and which sectors will grow in the future, that is founded on self-reinforcing discourses that suppress ambiguity and uncertainty, may lead research agencies not only to fund the same areas but perhaps the wrong areas too. That is, research (and economic and other benefits associated with research) may be damaged by misplaced certainty about the future. It is therefore appropriate to ask, among other things, by what process research agencies in fact come up with research priorities, whether they are consistent with our understanding of uncertainty about the future, whether they embody an understanding of how such priorities have been arrived at in the past (and the success of such prioritisation), and whether policies seek to achieve or reflect consensus, and potentially causing unnecessary, and unproductive duplication of research.

7.46 Notions of selectivity and exploitability have guided UK research policy for at least 20 years.[540] Yet we appear to have little reflection on whether that policy has been a success. To support and cultivate better public reasoning **there is a need for serious evaluation and assessment of past research policies, both of Government as a whole and of particular public funding bodies, to understand in what conditions, if any, selective approaches to support for biotechnology are plausible**. The study of returns to UK public and charity research in treatment of mental illness and cardiovascular disease sponsored by the MRC, Wellcome Trust and the Academy of Medical Sciences represents an effort of this kind. However, this study did not seek to conclude which benefits could be traced directly back to particular UK medical research, but made assumptions about what proportion of beneficial effects could be attributed (arbitrarily) to British research; it also assumed that secondary effects would be of the same scale as in the USA.[541]

7.47 The emergence of biotechnologies is subject to a variety of conditions, which, according to their own degrees of freedom, adapt to and respond to each other in a much more complex and unpredictable way than linear models of research policy assume. Openness, the construction of technological objectives as collective challenges, and coordination of research on the presumption of sharing benefits can help to address this, but only partially and often only in the context of national policy discourse that accepts the assumptions we have sketched out here. Although the importance of understanding uncertainty in R&D decisions has long been acknowledged and argued for, it remains under-discussed in research policy.[542]

7.48 Selectivity and commitment to particular technologies are not, in themselves, undesirable, but they are not always necessary and may be undesirable when they crowd out alternative approaches in conditions of substantial uncertainty.[543] Caution therefore recommends that **policy makers should consider adopting an approach to social objectives that fosters diversity of research approaches, not just within the particular domains of individual funding bodies but across physical and life sciences, and the social sciences, combined with selective conditions of innovation that involve social benefit rather than just market value**.[544] Diversity in approaches to R&D is needed within nations and across nations.[545] Policy

[539] For example: Cowen T (2011) *The great stagnation: how America ate all the low-hanging fruit of modern history, got sick, and will (eventually) feel better* (New York: Dutton Adult).

[540] Edgerton D and Hughes K (1989) The poverty of science: a critical analysis of scientific and industrial policy under Mrs Thatcher *Public Administration* **67**: 419-33.

[541] Health Economics Research Group (Brunel University), Office of Health Economics and RAND Europe (2008) *Medical research: what's it worth? Estimating the economic benefits from medical research in the UK*, available at: http://www.wellcome.ac.uk/stellent/groups/corporatesite/@sitestudioobjects/documents/web_document/wtx052110.pdf.

[542] A classic case is the work of Hitch and McKean for the US department of defence; see: Hitch CJ and McKean RN (1960) *The economics of defense in the nuclear age*, available at: http://www.rand.org/content/dam/rand/pubs/reports/2005/R346.pdf.

[543] See paragraph 2.33.

[544] See paragraph 6.33, with regard to halting innovation trajectories. We discuss how notions of social selection may be introduced into commercial biotechnology innovation in Chapter 9.

that allows freedom and flexibility in science would guard against ignorance of the mechanisms of innovation and scientific creativity.

7.49 There is an assumption that for each nation state there should be one public agency concerned with the funding of each particular type of research. Sometimes of course this is not the case, such as where areas of research are fundable by many agencies. Within Europe there is, of course, an overlapping European structure but it, too, is centralised, although the strengthened European Research Council has provided a welcome competitive stimulus to Framework programmes, with benefits to the UK research effort.[546] To justify centralisation, agencies point to the need to take a strategic overview, and to eliminate unnecessary duplication. Yet the costs of monopoly need to be taken into account as well: there can easily be a lock-in of policies that work poorly, with feedback mechanisms acting slowly. Although there *is* competition between research councils in the UK, that competition takes the form of vying for funding from Government, and of reducing commitment to interdisciplinary areas by passing responsibilities to another council. The key issue is to get competition to work to generate better quality claims for the importance of different research programmes and, most importantly of all, better outcomes in terms of research and of impact.

The 'Haldane principle' and policy control of research councils

7.50 For much of the 20th Century it has been fully accepted that most Government-funded research should be carried out under the direction of particular Government departments. However, increasing proportions of Government-funded research have been funded by research councils (see paragraph 7.10) under the supervision of the ministry for business (currently the Department for Business, Innovation and Skills (BIS)). Discussion of the actual policies and practices of the research councils and BIS has been coloured by an assumption that the policy should follow what is called the 'Haldane principle', which "states that decisions on general research should be made by researchers, free from political and administrative pressures."[547] This definition of the essential principle has been accepted by Government,[548] although only in relation to research funded by research councils inasmuch as they accept that researchers are best placed to determine detailed priorities. (By definition the determination of technical priorities requires expert knowledge, so this limited construction of the principle would be unreasonable to dispute.) As adopted today, the Haldane principle makes a very limited point about the role of researchers in running research council research programmes and similarly has very limited, if any, bearing on research policy.[549]

7.51 No UK government has ever supported a doctrine that researchers should decide public macro-level research policy. The nearest approach to such a doctrine was in the period 1916-64 when a small fraction of Government-funded research was overseen by research councils reporting to a non-departmental minister. These research councils were made up of independent figures of high standing from the worlds of industry and science. However, Government has never

[545] Stirling A (2011) Pluralising progress: from integrative transitions to transformative diversity *Environmental Innovation and Societal Transitions* **1**: 82-8.

[546] Currently an industrial perspective dominates the EU policy framework for a European bio-economy. A broad concept is being promoted at the public-relations level, but a narrower one apparently drives the EU's R&D priorities. Schmid O, Padel S and Levidov L (2012) The bio-economy concept and knowledge base in a public goods and farmer perspective *Bio-based and applied economics* **1**: 47-64. However, there was a little room created for research outside the dominant paradigm. Birch K, Levidow L and Papaioannou P (2010) Sustainable capital? The neoliberalization of nature and knowledge in the European "knowledge-based bio-economy" *Sustainability* **2**: 2898-918.

[547] Wakeham W (2008) *Review of UK physics*, available at: http://www.rcuk.ac.uk/documents/reviews/physics/review.pdf, p48. See generally Chapter 8 of that document for more information on the 'Haldane principle'.

[548] See, for example, the 2010 written ministerial statement on the Haldane Principle to the House of Commons, by the Minister for Universities and Science, David Willetts: House of Commons Hansard (20 December 2010) *c138WS*, available at: http://www.publications.parliament.uk/pa/cm201011/cmhansrd/cm101220/wmstext/101220m0001.htm.

[549] Department for Business, Innovation and Skills (2010) *The allocation of research science funding, 2011/12 to 2014/15: investing in world-class science and research*, available at: http://www.bis.gov.uk/assets/biscore/science/docs/a/10-1356-allocation-of-science-and-research-funding-2011-2015.pdf, p57.

suggested that decisions about specific research projects (namely those supported by research councils) should not be taken by researchers themselves and peer reviewers.[550]

7.52 In the absence of a clear, enacted principle, the question of who controls research policy, and with what aim, has continuing importance. Clearly expectations adopted by Government play a key role, but Government is not just politicians; it includes scientists, for instance, too.[551] It is highly suggestive, however, in view of our conclusions about the orientation of research policy towards economic growth,[552] that in recent years the research councils have been under the statutory control of BIS. Business therefore clearly plays a very powerful role within Government and research councils that may not be fully recognised, for example through the strong representation of business and industry 'users' of research within the policy structure. Representatives from business or industry are by far the main representatives of 'users' of research within the policy structure. At the time of writing, the TSB, for example, is made up primarily of business people; the councils of the research councils are made up of approximately equal numbers of academics and industry people, with the occasional representative of some other 'user'. The same pattern is usually repeated in many of the advisory panels, boards and groups associated with those organisations.[553]

7.53 Among the research councils, the concerns of other technology users and potential beneficiaries (and losers), and reflection on wider issues generally are addressed by sub-committees and panels constituted for that purpose. The Science and Technology Facilities Council has a largely private sector Economic Impact Advisory Panel, and an Advisory Panel for Science in Society. The experience of controversies around agricultural biotechnology convinced the BBSRC that it needed a forum to discuss societal issues surrounding its research, and it established the Bioscience for Society Strategy Panel which works closely with BBSRC's other Strategy Advisory Panels and reports regularly to the Council's Chief Executive. Its membership includes both academic social scientists and representatives of non-governmental organisations (e.g. the Soil Association). The MRC has an Ethics, Regulation and Public Involvement Committee, members of which include an academic biomedical ethicist. The EPSRC was somewhat later to act, but following a workshop in 2005 involving prominent scientists and social scientists, it established a Societal Issues Panel in 2007. This was to be an important body, reflected in its eminent membership, having the same status as the User Panel and the Technical Opportunities Panel (i.e. advising Council directly).[554]

7.54 There is some evidence that these panels have had a significant influence on the work of the research councils, although this influence is, by its nature, very difficult to ascertain.[555] It is possible to show that a number of more broadly focused activities that might not otherwise have taken place were initiated or commissioned by these panels: in the case of the EPSRC, one can point to a public dialogue about nanomedicine that had a direct influence on the way a funding

[550] The view that they *should* take such decisions has now been explicitly supported in a Written Ministerial Statement. See: House of Commons Hansard (20 December 2010) *c138WS*, available at: http://www.publications.parliament.uk/pa/cm201011/cmhansrd/cm101220/wmstext/101220m0001.htm.

[551] See Chapter 6, paragraph 6.57ff.

[552] See paragraph 7.10ff

[553] The membership of the TSB can be found at: http://www.innovateuk.org/aboutus/governingboard.ashx. Information on the general structure of the EPSRC can be found at: http://www.epsrc.ac.uk/about/governance/Pages/default.aspx. EPSRC 'strategic advisory team' membership can be found at: http://www.epsrc.ac.uk/about/governance/sats/Pages/default.aspx. The BBSRC general structure is outlined at: http://www.bbsrc.ac.uk/organisation/structures/structures-index.aspx, while information on its other boards and 'strategy panels' can be found at: http://www.bbsrc.ac.uk/organisation/structures/boards/boards-index.aspx and http://www.bbsrc.ac.uk/organisation/structures/panels/panels-index.aspx, respectively. The MRC's structure is explained at: http://www.mrc.ac.uk/About/Structure/index.htm and its advisory bodies, boards, panels and groups at: http://www.mrc.ac.uk/About/Structure/Advisorybodies/index.htm and http://www.mrc.ac.uk/Ourresearch/Boardpanelsgroups/index.htm.

[554] In 2011, the EPSRC reorganised its advisory structure, replacing its three advisory panels by a single 'strategic advisory network' but retaining some members of the Societal Issues Panel. See: EPSRC (2011) *Strategic Advisory Network*, available at: http://www.epsrc.ac.uk/about/governance/san/Pages/default.aspx

[555] See paragraph 5.12 for reflections on evaluation of qualitative influences more generally.

program was specified.[556] BBSRC and EPSRC jointly commissioned a dialogue around synthetic biology, the results of which were published in 2010 and noted as helpful in the 2012 *Synthetic biology roadmap*,[557] although the real impact on policy awaits further elaboration of themes under the current rubric of responsible innovation. The MRC displays an interest in engagement on its website.[558] BIS has a science and society strategy and also runs the 'Sciencewise Expert Resource Centre for Public Dialogue in Science and Innovation'.[559]

7.55 In discussion of engagement and responsible innovation, the argument is made that engagement is essential at an early stage of development. But what is usually meant is wider engagement, often of a limited sort, in the research policies of parts of governments or the EU. Candour is needed as to just how likely an intervention at this level will in fact change outcomes. The likelihood is that it would do very little. The reality is that key agendas are set elsewhere, such as in industry, and that any particular research council will have minimal influence. In other words, if the desired outcome is a real democratic debate and input into technological decisions, the measures needed to be enacted will be much more radical than anything currently practised. However, 'upstream' engagement can be very valuable to the extent that it can influence positively the quality of claims made by researchers for their research and set the context within which researchers construct justifications for their research. Our conclusion in that **research policy should be framed not by received assumptions but through continuous engagement with a broad range of societal interests and with the involvement of social actors who can bring understanding of these interests to the joint enterprise of constructing a public frame for research policy decisions**.

7.56 There were, in fact, good reasons for Lord Haldane's suggestion that some research that could affect a range of Government departments might be directed by semi-independent figures under a non-departmental minister. There might also be a good case for separating different kinds of research into different bodies, to avoid focusing on economic growth as the central theme of research policy. To achieve this, **consideration should be given to bringing Government research policy and funding bodies under a senior minister (i.e. of Cabinet rank) free from departmental responsibilities to ensure that research properly reflects all the objectives of Government, rather than those of a particular department**. Furthermore, in order to increase openness about the way in which biotechnology policy relates to social values, **there should be a clearly defined, written and published Governmental research policy against which detailed elements of departmental and other public research policies (such as the approach and methods of funding bodies) may be assessed**; this should not be produced, as it was formerly, by the Treasury.

Governance of charities

7.57 In contrast to the business focus of Government, membership of committees and boards within major charities that fund research is overwhelmingly comprised of academics[560] although subcommittees that focus on more technical problems such as drug discovery and technology transfer have a larger number of private sector members. The agenda for charity research funders is clearly focused on a particular social objective (the alleviation of ill health, for example, in contrast to economic growth) and that is bound up with a positive ethical mission.

---

[556] See, for example, Engineering and Physical Sciences Research Council (2009) *Nanotechnology programme*, available at: http://www.epsrc.ac.uk/SiteCollectionDocuments/other/LandscapeNano.pdf, p2 and HM Government (2010) *UK nanotechnologies strategy: small technologies, great opportunities*, available at: http://www.bis.gov.uk/assets/goscience/docs/u/10-825-uk-nanotechnologies-strategy, p35.

[557] See paragraphs 6.33 to 6.35.

[558] MRC (2012) *Public engagement opportunities for MRC research students/scientists*, available at: http://www.mrc.ac.uk/Sciencesociety/Publicengagement/index.htm.

[559] For the 'science and society strategy' see: Department for Business, Innovation and Skills (2012) *Science and society*, available at: http://www.bis.gov.uk/policies/science/science-and-society; for BIS's work in public dialogue see: Department for Business, Innovation and Skills (2012) *Public dialogue and policy making*, available at: http://www.bis.gov.uk/policies/science/science-and-society/communication-and-engagement/public-engagement-with-science/public-dialogue-and-policy-making.

[560] We reviewed the five largest UK medical charities by expenditure on research (according to the Association of Medical Research Charities): the Wellcome Trust, Cancer Research UK, the British Heart Foundation, Arthritis Research UK and Breakthrough Breast Cancer.

Thus, while there is a strong emphasis on the ethical conduct of research there is understandably less critical reflection on the overall objectives of the charity as its *raison d'être*.

7.58 All the major charities express an explicit position on the ethical aspects of the research they fund, although none mention 'social' impact specifically. In almost all cases, however, their requirements are couched in terms of adherence to pre-existing ethical and regulatory requirements (such as research ethics committee approval). The Wellcome Trust is an exception here: it publishes a large number of specific policies on various areas of research and, although the majority of the grant requirements relate to ethical and legal review by third parties, the Wellcome Trust has established a Standing Advisory Group on Ethics to consider and advise it on any major ethical issues associated with applications for funding that cannot be addressed through the standard procedures of local ethical review, such as the Home Office Inspectorate (for animal experiments) or research ethics committees (in the case of studies involving human subjects).

Conclusion

7.59 To capture the potential benefits from new discoveries and inventions in the biosciences is a difficult task and one that necessarily involves consideration of the exceptional levels of uncertainty and complexity, as well as the serious ethical and social issues that are involved. A central theme of this Report has been the need to realise that the way issues are framed is a critical influence on how decisions are made. An important purpose of this Chapter, therefore, has been to interrogate the kind of frames within which research policy is debated. The discourse on research policy has, however, shown difficulty engaging seriously with complex economic issues, let alone the closely related ethical and social issues. Part of the reason is doubtless that the main focus of discussion is on publicly-funded research policy, where the central concern is getting money from Government, and where it is felt that a focus on the economic benefits of research is what is required. Our examination suggests that, at least in the UK case, the principles informing Government research policy need to be better developed and made explicit, as a part of the publicly-determined frame for more detailed policy decisions.

7.60 In the absence of such principles, research policy is in danger of being determined through closed engagement between scientific, political and industrial elites, and, in the absence of unambiguous evidence, being framed by self-reinforcing but unexamined assumptions according to sectional values (such as economic growth, scientific excellence, shareholder value). These may participate in, but certainly do not exhaust, the social function of research policy. Government and research councils are trying to address this through efforts at broader engagement, some of which are now firmly institutionalised. However, this does not appear to be reflected in policy discourse at the highest level, which remains framed by traditional assumptions rather than social values, articulated principally within the economic growth paradigm and identified with particular technological trajectories.[561] To be clear, it is not merely that the concentration on economic growth obscures other values that are highly relevant, but that the basis for expecting economic growth from investment in biotechnologies is weak. In any case, the sort of engagement that is carried out, though valuable, tends only to inform decision making with one further dimension of proxy evidence, rather than to alter the nature or frame of decision making. More radical measures are therefore required.

7.61 The conventional framing of research policy is predisposed to expect benefits and to assume that securing them is a matter of funding the right area, one that therefore asks only what areas of research to support. Asking questions about who controls research, how research agencies come up with research priorities, whether they are consistent with our understanding of uncertainty, whether they are informed by past experience of such policies and whether they

[561] Evidence can be found in policy statements and speeches by Government Ministers, including those of the Prime Minister. See, for example, the 1 August speech on global health policy by the Prime Minister, available at: http://www.number10.gov.uk/news/global-health-policy.

aim to achieve or reflect consensus, suggests that it might be more appropriate to think of research policy as a process of encouraging the generation of new ideas and then of applying more reflective and broad-based ways of filtering and steering the development of those ideas. Funding conditions thereby act as one of a number of evolutionary constraints on technology development, rather than as an excuse to 'drive through' a chosen technology, riding roughshod over the uncertainties that must be confronted, including the uncertainty that a rejected alternative might, by an alternative path, have offered a more socially desirable outcome.

Chapter 8

Regulation

Chapter 8 - Regulation

Chapter overview

In this Chapter we sketch the main aims of regulation and argue that the difficult choices faced in the regulation of emerging biotechnologies are themselves examples of difficult choices made in most other important regulatory domains. Also in common with other domains, the regulation of emerging biotechnologies is framed predominantly by notions of risk of harm (in the dimensions of safety and security) and the likelihood of benefits. However, following from our conclusions in Chapter 3 that biotechnologies are characterised by radical uncertainty and that what constitutes risks and benefits has complex social dimensions (in addition to obvious physical harm) we argue that the focus on narrow conceptions of risk is inappropriate to the development of biotechnologies (as distinct from the use of biotechnology products).

A number of other characteristics of regulation, notably its national organisation, its preoccupation with national values and imperatives, its uneasy relationship with layers of extra-national regulation, its ambiguous accountabilities and its diffusion within a blurred advisory-policy-regulatory complex of governance institutions lead to the multiplication of potentially conflicting framings of biotechnology with no obvious privileged ground on which to resolve them. We identify a number of concrete problems to which this gives rise: problems of coordination and consistency, of voluntary and involuntary circumvention, and of democratic accountability.

We conclude that regulation cannot provide all the answers to securing benefits or averting harms from emerging biotechnologies, not least because emerging biotechnologies do not fit into risk-based regulatory models but require instead an approach guided by the virtue of caution which, in turn, requires a continuous and reflective engagement with broader societal interests.

Introduction

8.1 Regulators in the field of biotechnologies work under at least two (somewhat contradictory) pressures. On the one hand, regulation is expected to manage and mitigate the 'risks' associated with emerging biotechnologies; on the other, it is expected to do this while enabling, or even facilitating, the delivery of substantial, possibly transformative benefits. As we characterised them in Chapter 3, emerging biotechnologies present special challenges of uncertainty, ambiguity and transformative potential that are substantially settled in the case of established technologies. Emerging biotechnologies therefore often come up against regulatory conditions that are maladapted to them and that may unnecessarily inhibit certain trajectories or compound uncertainty.

8.2 In this Chapter we start by describing what might be called the 'dominant frame' in the regulation of emerging biotechnologies: a frame that stresses particular notions of 'risk' and that shapes regulatory language, decisions and practice. We provide examples of regulatory systems that focus particularly on 'risk' and argue that the special challenges of emerging biotechnologies show this risk-based frame to be unduly restrictive. Appropriate regulation involves both more and less than the identification and management of measurable 'risk': more because risks may be narrowly conceived; less because pursuing this focus may obscure other considerations of importance.

The purposes of regulation

8.3 Regulation is often understood as being animated by the aim of avoiding adverse consequences – physical, environmental, social or moral – of something that it is otherwise beneficial to do. These consequences, beneficial and adverse, are, of course, not necessarily of the same order. It is noteworthy that some biotechnologies are particularly associated with 'ethical regulation' that is not necessarily understood in terms of the protection of the interests of those directly involved (research participants, patients, consumers, the public, future generations, etc.) but goes to the public values of society more generally.[562]

[562] See, for example, the regulatory constraints imposed on human embryo research in the UK (see the 'Warnock report': Committee of Inquiry into Human Fertilisation and Embryology (1984) *Report of the committee of inquiry into human fertilisation and embryology*, available at:

Biosafety and biosecurity

8.4 A particularly influential set of concerns for the regulation of emerging biotechnologies has been physical and environmental harm described under the rubrics of 'biosafety' and 'biosecurity'. Of course, biosafety and biosecurity are not at all unique to emerging biotechnologies but they arise with particular force here because of the key characteristics of emerging biotechnologies: the way uncertainty, ambiguity and transformative potential simultaneously produce a culture of high expectations about benefits and high trepidation about harms, and where there are profound difficulties in predicting – or, indeed, identifying – either.

8.5 While the terms 'biosafety' and 'biosecurity' have no universally accepted definition and their meaning varies contextually,[563] they can be understood in the following ways:

- Biosafety relates to "the safe handling and containment of infectious microorganisms and hazardous biological materials",[564] applicable to humans, animals and the environment.

- Biosecurity relates to securing biological materials in the context of military and national security risks, for example in relation to biological warfare or biological terrorism. More generally, biosecurity can be understood as "the protection of living organisms from harmful effects brought about by other species, especially the transmission of disease".[565]

8.6 As a shorthand biosafety is sometimes thought of as being concerned with keeping hazardous biological materials away from people and biosecurity as being concerned with keeping people away from hazardous biological materials.[566] Biotechnologies present obvious biosafety issues given that they are intended to affect biological systems and some of these systems are capable of experiencing harm, either directly or indirectly.[567] However, what makes these issues particularly difficult to manage is the potential absence of a predictable, linear correlation between intervention and effect, and the uncertainty of the benefit or harm that might accrue. This is compounded as the combined effect of the special characteristics of emerging biotechnologies simultaneously create difficulties in anticipating the effect of possible regulatory designs or decisions ('locking in' or 'crowding out' a technology, for example).

---

http://www.hfea.gov.uk/docs/Warnock_Report_of_the_Committee_of_Inquiry_into_Human_Fertilisation_and_Embryology_1984.pdf) and in Europe Case C-34/10 *Brüstle v Greenpeace eV* (CJEU 18 October 2011), available at: http://curia.europa.eu/juris/liste.jsf?language=en&num=C-34/10#).

563 For example, biosecurity could be understood as a subset of biosafety: a procedure designed to limit the possibly of pathogens being acquired for criminal purposes could be easily understood as part of basic laboratory biosafety measures for the containment of hazardous material. In turn, biosecurity has been described as becoming "the master frame for debates about threats to human, animal, and plant-based ecologies and the policies and practices developed to anticipate and mitigate risk." Maye D, Dibden J, Higgins V and Potter C (2012) Governing biosecurity in a neoliberal world: comparative perspectives from Australia and the United Kingdom *Environment and Planning A* **44**: 150.

564 Department of Health and Human Services, Centers for Disease Control and Prevention and National Institutes of Health (2009) *Biosafety in microbiological and biomedical laboratories: 5th edition*, available at: http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf, p1.

565 Lackie J (Editor) (2007) *Chambers dictionary of science and technology* (Edinburgh: Chambers), p123. However, there is no single accepted definition of the term (see: Health and Safety Executive (2007) *Final report on potential breaches of biosecurity at the Pirbright site 2007*, available at: http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf, p10). However, it may be taken to imply both the "containment of ideas and information as well as bio-agents" (Sture JF (2010) *Dual use awareness and applied research ethics: a brief introduction to a social responsibility perspective for scientists*, available at: http://www.brad.ac.uk/bioethics/media/SSIS/Bioethics/docs/Dual_Use_and_Soc_Resp_Guidance_FINAL.pdf) as is the case, for example, with knowledge concerning the synthesis of pathogens. See: Herfst S, Osterhaus ADME and Fouchier RAM (2012) The future of research and publication on altered H5N1 viruses *Journal of Infectious Diseases* **205**: 1628-31.

566 Sture JF (2010) *Dual use awareness and applied research ethics: a brief introduction to a social responsibility perspective for scientists*, available at: http://www.brad.ac.uk/bioethics/media/SSIS/Bioethics/docs/Dual_Use_and_Soc_Resp_Guidance_FINAL.pdf, p7.

567 The objective of the Cartagena Protocol on Biosafety is to ensure an "adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity…" (Article 1). United Nations (2000) *Text of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity*, available at: http://treaties.un.org/doc/Treaties/2000/01/20000129%2008-44%20PM/Ch_XXVII_08_ap.pdf.

8.7 An example of such a risk-based regulatory system can be found in the European framework for the contained use and deliberate release of genetically modified organisms (GMOs).[568] It is based primarily on risk assessment procedures relating to physical harm. Both contained use and deliberate release require specific assessment procedures to be followed before authorisation is given:[569]

- An assessment of contained uses should take into account issues including disease to humans, animals and plants; and deleterious effects due to the impossibility of treating (or providing a prophylaxis for) a disease. The relevant European Directive notes that "[t]he first stage in the assessment process should be to identify the harmful properties of the recipient and, where appropriate, the donor micro-organism, and any harmful properties associated with the vector or inserted material, including any alteration in the recipient's existing properties."[570]

- An environmental risk assessment for deliberate release has the objective of identifying and evaluating "potential adverse effects of the GMO, either direct and indirect, immediate or delayed, on human health and the environment".[571]

8.8 The 'scientific' nature of risk assessments in this area are often emphasised. For example, the UK Department for Environment, Food and Rural Affairs (Defra) notes that "[u]nder European Union (EU) legislation, GMOs, including genetically modified crops, can only be released into the environment if a science-based risk assessment shows that safety will not be compromised";[572] the European Food Safety Authority states (EFSA) "[g]enetically modified (GM) foods can only be authorised in the European Union if they have passed a rigorous safety assessment".[573] Although EFSA does not actually authorise GMOs – this is done by the European Commission – it does provide what it describes as "scientific advice" through the GMO Working Panel, which is comprised of "independent scientific experts" who release assessments based on "scientific dossiers".[574]

The 'dual use' problem

8.9 The term 'dual use' is intricately linked with the issue of biosecurity and is applied to the tangible and intangible features of a technology that enable it to be applied to both hostile and peaceful ends with no, or only minor, modifications.[575] The US National Science Advisory Board for Biosecurity (NSABB)[576] describes dual-use research that raises concern as "research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, agricultural crops and other plants, animals, the environment or materiel."[577]

8.10 To some extent, all technologies (for example, metallurgy, explosives, electronics, and nuclear energy) have been used for hostile purposes.[578] However, some have argued that modern biomedical research is 'dual use' in a way that is not the case with regard to, for example,

---

[568] 'Contained use' generally refers to work in research laboratories while 'deliberate release' refers to activities such as placing a product on the market.
[569] Article 6(2) Directive 90/219/EEC on the contained use of genetically modified micro-organisms and Article 4(2) 2001/18/EC on the deliberate release into the environment of genetically modified organisms, respectively.
[570] Annex III, Directive 2009/41/EC on the contained use of genetically modified micro-organisms (recast).
[571] Annex II, Directive 2001/18/EC.
[572] Defra (2012) *Genetic modification (GM)*, available at: http://www.defra.gov.uk/environment/quality/gm.
[573] European Food Standards Agency (2012) *Genetically modified organisms*, available at: http://www.efsa.europa.eu/en/topics/topic/gmo.htm.
[574] Ibid.
[575] McLeish C and Nightingale P (2005) *Strengthening the Biological Weapons Convention briefing paper No 17 (second series) – effective action to strengthen the BTWC regime: the impact of dual use controls on UK science*, available at: http://www.sussex.ac.uk/Units/spru/hsp/documents/Mcleish%20pubs%20BP_17_2ndseries.pdf, p4.
[576] The NSABB is a US "federal advisory committee chartered to provide advice, guidance, and leadership regarding biosecurity oversight of dual use research". See: National Institutes of Health (2012) *About NSABB*, available at: http://oba.od.nih.gov/biosecurity/about_nsabb.html.
[577] National Institutes of Health (2012) *Dual use research and dual use research of concern*, available at: http://oba.od.nih.gov/biosecurity/nsabb_faq.html#NSABB_FAQ002.
[578] Meselson M (2000) Averting the hostile exploitation of biotechnology *The CBW Conventions Bulletin* **48**: 16-9, p16.

nuclear materials technology, insofar as the "underlying research and technology base is available to a rapidly growing and increasingly international technical community".[579] For example, "pathogens listed by the Government as potential agents for terrorists are used in thousands of clinical and diagnostic laboratories."[580]

8.11 Regulatory decisions made around biosecurity and dual-use research touch on a number of areas: health, security, academic freedom, international trade and scientific and technological development. A commonly discussed biosecurity concern is the possibility of limiting research on the creation of particular pathogens from scratch, or work on increasing virulence in an attempt to reduce the likelihood of the information being used by hostile non-state actors or rival states. For example, NSABB recommended in 2011 that experimental evidence relating to a highly pathogenic avian influenza virus subtype acquiring the ability to transmit via aerosols between ferrets should not be published.[581] In 2012, NSABB concluded that knowledge generated by the research "could conceivably be directly misused to threaten public health or national security."[582] There are significant uncertainties on both sides in such decisions: the likely threat to national or global security is hard to quantify and the longer range health benefits of relatively early stage research are difficult to gauge.

Relevance to issues concerning emerging biotechnology

8.12 There are distinctive approaches in the regulation of biotechnologies (and applied biotechnology research) depending on whether their context of application is medical or non-medical, and whether their primary perceived effect is on human health or on the environment. What is more important than technical risk assessment in relation to emerging biotechnologies is to explore the meaning of the risks and levels of uncertainty. For example, there were, and remain, considerable ambiguities associated with the implementation of GM technologies, especially in relation to food crops: technically accurate risk assessments relating to acceptable levels of cross-contamination between GM and non-GM crops, or the likelihood or physical harm to human recipients of the resulting food, fail to take adequate account of the level of polarisation in societal attitudes to the technology. As a result, many conflicting – sometimes irreconcilable – value judgments applied by different parts of society are simply excluded from the formal regulatory procedures for decision making. Such exclusions can ultimately destabilise the expected technological pathway for which regulation is designed. Whether or not they do so may depend partly on how the different framings are established in society and on how judgments are amplified in the social discourse surrounding the technology. (For example, social opposition to GM crops and foods was effectively amplified; principled opposition to human embryo research has remained marginal.)

8.13 The (non-)introduction of GM crops into the UK is often highlighted as an example of a failure to commercialise a new technology. Much has been said in relation to synthetic biology and nanotechnology in terms of how to avoid the 'pitfalls' encountered by those who went though the same process with GM crops in the late 1990s and early 2000s.[583] To some extent, these issues could have been avoided (which does not necessarily mean a different outcome would have resulted) if there had been a more sophisticated appreciation of the complex nature of the uncertainties and ambiguities associated with the technology: simply noting the safety of a technology within particular defined boundaries does not necessarily address the concerns of those objecting to its introduction if there is a fundamental disagreement about the significance

[579] Stern J (2002/3) Dreaded risks and the control of biological weapons *International Security* **27**: 89-123.
[580] Ibid, p95.
[581] Herfst S, Osterhaus ADME and Fouchier RAM (2012) The future of research and publication on altered H5N1 viruses *Journal of Infectious Diseases* **205**: 1628-31. See also Box 3.1.
[582] National Science Advisory Board for Biosecurity (2012) *Findings and recommendations: March 29-30, 2012*, available at: http://oba.od.nih.gov/oba/biosecurity/PDF/03302012_NSABB_Recommendations.pdf, p5.
[583] See, for example: Sciencewise (2011) *Listening or explaining? Avoiding a deficit approach to public engagement in synthetic biology*, available at: http://www.sciencewise-erc.org.uk/cms/listening-or-explaining-avoiding-a-deficit-approach-to-public-engagement-in-synthetic-biology.

of its effects. However, despite this, the abandonment of the public dialogue on GM food in 2010 seems to indicate that these lessons have not been taken to heart by regulators.[584]

8.14 There is often no intellectually compelling way of demonstrating that one set of priorities or concerns should 'trump' others. A resolution depends to a great extent on a process of reflection and wide engagement in which ethical choices will often have to be confronted. Issues of risk are important, but must be dealt with as part of the construction of a shared public understanding of the uncertainties and ambiguities associated with emerging biotechnologies. We return to this below, when we consider the issue of the precautionary principle, which has been so central to technology innovation. But having recognised the multiple difficulties of regulation we first explore what a more sophisticated understanding of regulation does to the way it should function in the domain of emerging biotechnologies.

The organisation of regulatory systems

8.15 We understand 'regulation' as being the embodiment of the decisions made by regulators, both individuals who establish regulatory frameworks and institutions (legislators, etc.) and those regulatory bodies with discretionary powers to interpret and inform the rules they exist to apply.

8.16 Some of the most revealing evidence we received came during a discussion with a cross-section of practising regulators and experts on the institutional structure of regulation as it relates to emerging biotechnologies, with particular reference to the connections between national and international regulatory bodies.[585] This identified some key features of regulatory systems that influence emerging biotechnologies.

8.17 First, regulation is heavily national in organisation. Conversely, the biotechnology industries are global in range, the innovation systems that underpin those industries routinely transcend national boundaries and the mechanisms for transmission of knowledge – notably in organised scientific communities – now overwhelmingly use the single universal scientific language, English. Nevertheless, regulatory authorities, and the networks in which these authorities operate, retain very distinctive national identities. This is not surprising as, despite the importance of multinational corporate actors and the increasingly global organisation of innovation systems, key institutions remain embedded in particular national territories. The most obvious example of such embedding is provided by universities, which remain culturally, politically and financially dependent on nation states.

8.18 Second, regulation is heavily national in preoccupations and sensibilities. One of the most important features shaping regulation of emerging biotechnology is recurrent preoccupation with its safety and ethical implications. However, the shape and content of these preoccupations varies remarkably by territory and is plainly woven around the workings of national governing systems and national cultural understandings: from some territories, such as the UK and Europe, the uncertainties surrounding GM technology have been a significant influence on the trajectory of the technology; for others, such as the US, the issue has been of marginal importance. For some territories the ethical implications of innovations in human embryonic stem cell technology appear to have created considerable barriers to research; for others (the UK included) the consequences of ethical arguments seem to have facilitated research by putting in place clear regulatory frameworks that provided legal clarity and security for researchers.[586]

---

[584] See: Sciencewise (16 September 2010) *Announcement by science minister on GM public dialogue*, available at: http://www.sciencewise-erc.org.uk/cms/food-the-use-of-genetic-modification-a-public-dialogue, especially the letter of resignation from the steering group of Professor Brian Wynne. In a later publication, Wynne (writing with Doubleday) identified the development of a new and fragile imaginary following BBSRC's *Crop Science review* "to a more holistic, diversely grounded, and flexible portfolio of future scientific, agricultural and social possibilities and priorities." Doubleday R and Wynne B (2011) Despotism and democracy in the United Kingdom: experiments in reframing citizenship, in *Reframing rights: bioconstitutionalism in the genetic age*, Jasanoff S (Editor) (Cambridge, Massachusetts: MIT Press), p255.

[585] Oral evidence from the fact-finding meeting on policy, regulation and governance, held by the Working Party, 8 July 2011.

[586] It is generally understood that in the US, ethical considerations were the reason for the restriction of federal funds for stem cell research. However, in responding to our consultation, Cesagen (ESRC Centre for Economic and Social Aspects of

8.19 Third, while national in organisation and culture, regulation is set within multiple layers of extra-national organisation.[587] A common term to describe this situation is to characterise it as 'multilevel', which it undoubtedly is in the most obvious sense. As with any multilevel system, issues of hierarchy and coordination are critical to the way regulation is prasticed. However, the bloodless language of multilevel regulation fails to convey the forces moving and shaping the regulatory system. One example of such a profound force makes this point clear. In the last generation the European Union has emerged as a major actor in this regulatory system, which has given rise to a whole distinct set of preoccupations and problems. Some echo national themes, some are distinctive to the organisational culture of European Union institutions and some reflect the extent to which the Union attempts to speak as a voice for collective Union interests in the economic competition which partly powers biotechnology innovation systems. This imports a number of issues into the regulation of emerging biotechnology, such as the problem of the unreasonable burden placed on innovation to advance common economic interests,[588] and problems of public accountability and democratic control where administrative power is shared between technocrats and corporate interests.

8.20 Fourth, although populated by public institutions, the regulatory system is, in practice, a 'mixed economy' of the public and the private. In a sense all regulation is a partnership between public regulators and private actors. Even the most extreme 'command' systems require some partnership between regulator and regulated. However, in the case of emerging biotechnologies the relationship is particularly important as many of the most significant institutions in the innovation system are private corporations. Others, like university researchers, operate within the regulatory frameworks laid down by public institutions (universities, research funding institutions) or within privately negotiated frameworks of rules governing a complex array of issues ranging from scientific integrity to prudential issues of safety and security. Indeed, some of these are considered in our separate chapters on the research process (Chapter 6) and the process of commercialisation of innovation (Chapter 9). At least since the Asilomar conference on recombinant DNA in 1975 there has been recognition among researchers that taking a responsible self-organising approach in new fields of research may forestall or delay public regulation and, indeed, develop an inclusive social discourse with aspirations to make public regulation unnecessary.[589]

UK regulatory systems

8.21 The UK has, in recent years, been marked by a lack of stability and clarity in the regulation of biotechnologies, reflecting the wider instability of regulatory institutions in the UK. The importance of the national setting of regulatory institutions means that changes in the regulatory system in the UK are particularly important for one group of readers of this Report: those who work within the UK. The picture here, as elsewhere, is mixed, involving a number of government departments, and statutory and non-statutory, executive arm's length and 'expert' bodies.

Genomics) noted that they were unaware of any hard evidence "clearly showing (for example in terms of publications, or industry success) that the restrictions on federal funding in the US have necessarily hampered research in this area".

[587] See, for example, the range of international agreements and organisations concerned in some way with biotechnology. For example: the World Trade Organization, the WHO, the Cartagena Protocol on Biodiversity, the UN Food and Agriculture Organization, the Trade-Related Aspects of Intellectual Property Rights Agreement, the Biological and Toxin Weapons Convention, in addition to the various biotechnology related organisations of the European Union.

[588] This is illustrated by the experience of the Lisbon process. See, for example, the heavy emphasis on innovation as a means of achieving economic progress described in European Council (2000) *Presidency conclusions: Lisbon European Council – 23 and 24 March 2000*, available at: http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/ec/00100-r1.en0.htm.

[589] The Asilomar conference led to guidelines on recombinant DNA technology that restarted research after a previous voluntary moratorium, although this was subsequently criticised by some for being too focused on particular dimensions of risk (such as the decision not to include ethical and legal concerns). For two brief summaries, see: Berg P and Singer M (1995) The recombinant DNA controversy: twenty years later *Proceedings of the National Academy of Sciences* **92**: 9011-3 and Berg P (2004) *Asilomar and recombinant DNA*, available at: http://nano.z9i.com/files/Asilomar%20and%20Recombinant%20DNA.pdf; this approach has been developed by the current 'responsible innovation' movement that has characterised self-organising initiatives such as the Responsible Nano Forum (see: http://www.nanoandme.org/home) and successive synthetic biology conferences.

8.22 Statutory regulators who work in a particular sector, such as the Human Fertilisation and Embryology Authority (HFEA, which regulates research involving human embryos and therefore holds the keys to the door of much stem cell research), have provided some stability and appreciation of issues within a particular sector, a value evidenced by support from even some of its most consistent critics in the face of current threats to its existence as an independent regulator.[590] This has made it possible to introduce a measure of regulatory flexibility in this an area where technologies continue to emerge, albeit flexibility that periodically comes up against the need to amend or clarify the framework legislation.[591]

8.23 Other, more broad-based and traditionally 'administrative' regulators – such as the UK's Medicines and Healthcare products Regulatory Agency (MHRA), which regulates drugs and medical devices, may have less flexibility. It has been put to us in evidence that regulatory authorities in the UK tend to interpret international and European rules more restrictively than in other countries, leading to a well intentioned, but inflexible and sometimes counterproductive, regulatory environment.[592] For example, it was suggested that the UK's capacity to produce vaccines for new strains of influenza is severely hampered by regulation that focuses on processes rather than products: it was argued that, although the seed strains for flu vaccines can be produced in a matter of weeks using genetic engineering techniques, laboratories in the UK use slower, conventional methods because the genetic modification of influenza strains for this purpose is impeded by the regulatory system, despite the products of both methods being genetically indistinguishable. On one view, this regulatory approach may inhibit the development of novel approaches (it can be understood as an example of regulatory influence helping to lock-in a sub-optimal technology); on another, the alternative of regulating products rather than processes may be more cumbersome and complex, and vulnerable to inconsistency.

8.24 Elsewhere the picture is even more diffused. A number of regulatory functions are exercised by groups that have grown out of advisory committees set up, *ad hoc*, to advise Government departments on specific issues: thus the Home Office Animal Procedures Committee 'advises' on the use of animals in research, and the Advisory Committee on Releases to the Environment 'advises' on GM field trials, where the power of approval is nominally retained by ministers, although, in practice, ministers tend to defer to the technically competent though democratically unaccountable committees.[593] The lines of accountability of these bodies are often as obscure as their origins, and they may be beholden to officials rather than ministers, with their membership drawn from nominated experts rather than via open public appointments. These committees in reality often, although not always, have a mixture of advisory and licensing or regulatory functions and, although nominally offering scientific expertise, may also extend into offering public policy and ethical advice.[594]

8.25 Beyond committees that advise ministers who formally hold regulatory powers are further officially sanctioned and respected bodies. However, these bodies are not part of any formal

---

[590] It is proposed, and powers have been secured in the Public Bodies Act 2011 (section 5 and Schedule 5), that along with a number of other 'quangos' the HFEA's functions should be merged into other general regulators. This proposal comes after plans to merge the HFEA and HTA into a proposed Regulatory Authority for Tissue and Embryos were abandoned in the face of opposition in 2007 (see: Joint Committee on the Human Tissue and Embryos (Draft) Bill (2007) *Human tissue and embryos (draft) Bill*, available at: http://www.publications.parliament.uk/pa/jt200607/jtselect/jtembryos/169/169.pdf, at p34ff). See also the Draft Care and Support Bill, which would amend the Public Bodies Act 2011 to allow for the abolition of the HFEA and the HTA (section 75); this proposal is, however, subject to a public consultation which closed 28 September 2012, the results of which had not been published at the time of writing. See: Department of Health (11 July 2012) *Draft Care and Support Bill published*, available at: http://www.dh.gov.uk/health/2012/07/careandsupportbill and Department of Health (28 June 2012) *Consultation launched on fertility and human tissue regulators*, available at: http://www.dh.gov.uk/health/2012/06/consultation-regulators.

[591] As in the case of human 'cloning' techniques and the creation of 'human admixed embryos'.

[592] Oral evidence from the fact-finding meeting on policy, regulation and governance, held by the Working Party, 8 July 2011.

[593] A striking counterexample was offered by the refusal, in 2009, of the then Home Secretary Alan Johnson, to accept the advice of the Advisory Committee on the Misuse of Drugs regarding relative classification of alcohol, tobacco and illegal drugs, which, on the principle that this was treated by the Government not merely as a technical issue but one of broader social policy, might be applauded. The lie was given to the purely technical and advisory role of the SAC by the fact that this incident threw the entire SAC system into turmoil, resulting in a review by the GCSA and the development of new 'rules of engagement' re-reinforcing independence, tempered by responsibility (see: Government Office for Science (2012) *Principles of scientific advice to government*, available at: http://www.bis.gov.uk/go-science/principles-of-scientific-advice-to-government) but not before drawing in the media and external bodies like the Royal Society.

[594] For the origins and accountabilities of SACs, see footnote 480.

structure of accountability, but are able to exert influence directly in relation to the field of practitioners. These include bodies like the UK Genetic Testing Network, which advises on genetic tests for use in the National Health Service, self-described public benefit organisations such as the BioBricks® Foundation, and membership bodies and trade organisations (e.g. the British In Vitro Diagnostics Association[595]) that produce voluntary and self-addressed standards and guidelines, alongside international organisations such as the Organisation for Economic Co-operation and Development or the World Health Organization.

Problems of the regulatory system

8.26 In arriving at a system of regulation there are always dilemmas to be confronted and trade-offs to be made. These are not unique to emerging biotechnologies. In fact they are strikingly common. What is clear is that regulation of novel biotechnologies has itself to develop and adapt to the technologies, but in a way that cannot leave those technologies unaffected. Furthermore, it is unlikely to do so in perfect step with the technology. This means that biotechnologies may emerge under pre-existing regulatory systems that are not well adapted, and may be slow to adapt to them (gene-based vaccines and the MHRA, for example), or outside them entirely. Either of these conditions may increase the uncertainty or even result in crowding out an emerging biotechnology. Since the technologies serve potentially important social aims, questions of regulatory design may therefore also raise important issues of social choice.

Problems of coordination

8.27 The search for effective coordination has been described as the search for the 'philosopher's stone' of regulation.[596] As this image suggests, the search has proved elusive, and emerging biotechnologies are no exception. The fundamental reason for this is that there is no intellectually coercive solution to the problem of how to coordinate the complex institutions of biotechnology regulation, which may be national, supranational, public and private. The 'problem' of coordination is, in essence, a dilemma: in designing or assessing regulatory institutions there is an obligation to choose between central control (with its attendant surveillance advantages but control inefficiencies) and distribution of authority (with its attendant control advantages but surveillance problems), with a potential result being oscillation under the pressure of crisis between centralisation and distribution of regulatory authority.

Problems of evasion, circumvention and involuntary rule breach

8.28 Systems of regulation are systems of surveillance and restraint. If individuals and institutions were completely compliant with both the letter and spirit of rules no institutions of regulation would be required other than those needed to formulate the rules in the first place. The very complexity of the regulatory systems governing emerging biotechnologies shows that the regulatory system is constructed on the premise that evasion (the conscious breach of rules), and circumvention (the creative avoidance of restrictions short of rule breaking), are constants in the innovation system. We do not have to imagine a world of recalcitrant rule evaders to see why surveillance is needed. Many breaches of regulation are due to the often dizzying complexity of rules and the problem of matching particular sets of rules (which must be confirmed at one moment in time) with the constant flow of new issues produced by the dynamism of the world of biotechnology research. One of the points made to us during our evidence gathering meetings, by entrepreneurs in particular, was the intimidating complexity of

[595] See, for example, The British In Vitro Diagnostics Association (2008) *BIVDA code of conduct*, available at: http://www.bivda.co.uk/Portals/0/Documents/BIVDA_CoC_leaflet.pdf. Expulsion from a professional body can be a powerful regulatory measure, depending on the level of the recognition of membership and the extent to which membership or accreditation in the case of services and facilities is given a formal acknowledgment in other regulatory systems.

[596] Seidman H (1975) *Politics, position, and power: the dynamics of federal organization* (New York: Oxford University Press), p190.

the regulatory landscape faced by small start-up firms, which lack the resources of, for example, the pharmaceutical giants.[597]

Problems of democratic accountability and public engagement

8.29 Debates about public engagement and democratic accountability in the domain of emerging biotechnologies often turn around the divergent fears and perceptions characteristic of specialist and public perspectives, exemplified by the case of GM crops and public concerns about the ethical consequences of particular innovations or particular scientific practices (such as stem cell research). This follows from something examined above: the framing of regulatory issues in terms of risk. It arises from the central features of emerging biotechnologies identified in this Report, features that arouse simultaneously popular feelings of trepidation and expectation. During discussions with UK regulators concerning the issue of public involvement, the 'problem' of how to manage public perceptions of innovations was raised, unsurprisingly given the experience around the prospect of introducing GM crops to the UK.[598] These are only particular instances of a recurrent set of issues faced in the domain of emerging biotechnologies: how to ensure that the 'public' has an appropriate level of involvement with decisions about the public good, in a domain marked by powerful corporate interests, technocratic regulators who routinely use a vocabulary accessible only to the initiated, and in multinational institutions that suffer from a considerable democratic deficit.

Problems of 'breadth' and 'depth'

8.30 Another dilemma is between narrowly focused regulation involving expert bodies and sector-specific regulators, and more generic regulation that may apply well-established procedures. Technology-specific regulation provides understanding and sensitivity to the situated issues, and allows constant regulatory inventiveness to adapt to uncertainty, although it requires a higher level of autonomy (and therefore raises separate questions of accountability) and can become framed by shared interests between regulators and the regulated (for example, where the regulator's income or existence is linked to the activity of those regulated). It may also be powerless in the face of a technological trajectory that escapes its remit.[599] Conversely, broader, more generic regulators may apply rules inflexibly and be less adaptive to new technologies[600] but be capable of maintaining broader alignments and consistencies.

Problems of balancing 'soft' and 'hard' regulation

8.31 An almost unending problem of regulatory design is that of striking the right balance between 'soft' and 'hard' regulation: between regulation that typically relies on voluntary codes and autonomous professional institutions, and regulation that relies on law and the unique power of the state to enforce it. 'Hard' regulation may be more resource intensive, involving activities that may include licensing, monitoring, inspection and enforcement, but this is not necessarily the case, and in the UK there is now an expectation that the cost of regulation should be met by those regulated, who are benefitting from the service provided by regulators. To express the distinction between hard and soft regulation as this dichotomy is to see immediately that no simple choice between 'soft' and 'hard' is possible. Any conceivable system is a mixture of the two: as we noted above, in the last analysis even the most hierarchical form of command regulation depends to some degree on voluntary compliance; and effective systems of 'soft' regulation (such as those organised by professional bodies) depend ultimately on the 'bite' of some disciplinary sanctions. There is no problem of working simultaneously with hard and soft regulation. The big problem is deciding what in the case of any particular process is the most effective combination. Everything we have said above about regulation – its often multi-level character, the influence of national settings – suggests that the balance cannot be struck by

[597] Oral evidence from the fact-finding meeting on intellectual property, innovation and markets, held by the Working Party, 24 June 2011.
[598] Oral evidence from the fact-finding meeting on policy, regulation and governance, held by the Working Party, 8 July 2011.
[599] The longitudinal regulation of human embryonic stem cells in the UK presented such a challenge in the 2000s.
[600] See paragraph 8.23.

invoking a formula, but must depend on the contingencies of the particular process being regulated.

Reframing regulation in emerging biotechnology

8.32 Most important choices in regulation have the character of dilemmas: they involve choosing between alternatives neither of which is ideal. As the earlier discussion shows,[601] there is – when identifying appropriate regulatory approaches for biotechnologies – a tendency to concentrate on what regulation is arguably most effective at, namely the management of a particular understanding of 'risk'. Understanding of the nature and level of risks may well help to identify a provisionally appropriate response to these dilemmas in the case of relatively well established technologies, where the technologies are embedded in stable public frames. However, it is little use in resolving them where the risks are not well characterised, and their gravity and significance are neither stable nor understood, as is the case with emerging biotechnologies. It is important, therefore, to see the shaping of regulation of emerging biotechnologies within a context of responsible innovation that involves a much broader public reflection on the ethics, acceptability and appropriateness of specific principles, practices and measures to regulate them.[602]

Reframing (pre)caution

8.33 If regulation of emerging biotechnology requires the balancing of competing, and sometimes opposing, considerations, there are several ways in which the theory and practice of regulatory design can be distorted to inhibit this. A good example of this is provided by the functioning of perhaps the most well known principle governing regulation, not only in the domain of emerging biotechnologies but in technology generally: the precautionary principle.[603]

8.34 At root, interest in approaches of this kind to regulation arises from realisations about the limits of narrow, risk-based approaches when operating under conditions of uncertainty and ambiguity. Much criticism of the regulatory use of precaution simply ignores these limits and insists that risk assessment is universally applicable.[604] But no matter how inconvenient it may be, the calculation of an optimal balance between benefits and harms is not feasible under conditions of uncertainty and ambiguity.[605] On the other hand, much advocacy of precaution is associated with positions on particular technologies (like bans or phase outs), which can equally ignore uncertainties and ambiguities associated with the alternative courses of action (including maintaining the *status quo)* that are available. Partly because policy discussions of the role of precaution in technology regulation have tended to be polarised, we have formulated our 'virtue

[601] See paragraphs 8.7 to 8.8.

[602] 'Responsible innovation' is developing as a major theme within the biosciences and technology more generally but has not come to fruition despite being presaged in various places (such as the UK's synthetic biotechnology roadmap – see paragraphs 6.33 to 6.35). See, for example, the forthcoming work commissioned by the EPSRC on this topic: Stilgoe J, Owen R and Macnaghten P (2012 – forthcoming) *An outline framework for responsible innovation*. At an EU level, the theme has been taken up under the Science in Society Programme of DG Research and Innovation (see: European Commission (2012) *Policy and strategy documents*, available at: http://ec.europa.eu/research/science-society/index.cfm?fuseaction=public.topic&id=1401) as well as by the European Group on Ethics (see the relevant papers from the meeting of 20 September 2011: European Group on Ethics (2011) *Meetings*, available at: http://ec.europa.eu/bepa/european-group-ethics/bepa-ethics/ec-international-dialogue-bioethics/meetings_en.htm).

[603] The first statement of the precautionary principle in an international treaty may be found in the United Nations Conference on Environment and Development (1992) *Rio Declaration, Annex I*, available at: http://www.un.org/documents/ga/conf151/aconf15126-1annex1.htm, Principle 15; a large literature has developed around this principle and its various forms as restated in other influential documents and instruments. See also: Harding R and Fisher EC (Editors) (1999) *Perspectives on the precautionary principle* (Sydney: Federation Press); de Sadeleer N (2002) *Environmental principles: from political slogans to legal rules* (Oxford: Oxford University Press).

[604] Jones JS and Von Schomberg R (Editors) (2006) *Implementing the precautionary principle: perspectives and prospects* (Cheltenham: Edward Elgar Publishing).

[605] Jaeger CC, Renn O, Rosa EA and Webler T (2001) *Risk, uncertainty, and rational action* (London: Earthscan).

of caution' under a distinct but related rubric,[606] as a mode of reflection that may give rise to distinct principles when applied to different circumstances.

8.35 The most rigorous (and commonsense) solution to both problems is to acknowledge that precaution should not be understood as a 'rule' upon which decisions may be based, like those promoted by risk assessment or rational choice theory.[607] Indeed, it is a consequence of uncertainty and ambiguity that definitive rules of this kind, despite their expediency, cannot be formally applied.[608] Instead, caution should be understood as a process to be undertaken when regulation is judged to be especially subject to intractable uncertainty.[609] More specifically, it offers a way to help regulators learn how to respond more appropriately when operating under the conditions of uncertainty and ambiguity.[610] This is best achieved by 'broadening out' the process of regulatory appraisal in a variety of different ways, such as to explore and compare more extensively the contrasting implications of alternative possible innovation trajectories (including that of 'business as usual').[611]

8.36 In particular, then, giving effect to the principle of caution involves the comparison of a wider range of policy options than simply saying 'yes' or 'no' to a single specific proposed technology. These may include other technologies for the same purpose or other social or organisational practices that may offer similar ends.[612] The range of issues considered is also broadened out, going beyond the small set of direct or immediate factors that are most readily quantified (e.g. as risks), to include potential benefits and justifications as well as the tolerability of projected possible harms,[613] including, for example, how to balance avoidance, resilience and remediation in the face of adverse impacts. The trend for increased use of public engagement by regulators can contribute positively here in identifying and clarifying various different options and perspectives concerning how precaution can be incorporated into social choice and regulatory practice[614] (although here, too, there is institutional learning:[615] for example, the design of subsequent dialogues on nanotechnology and synthetic biology appears to have learned from the experience of earlier engagements around GMOs).

8.37 When regulatory appraisal becomes more critical about the quality of types of knowledge about benefits and harms, a series of other qualities of emerging biotechnologies (that might otherwise be neglected in risk-based approaches) becomes relevant. This includes the extent to which the effects of different technologies, or the developmental trajectories of the technologies themselves, may be reversible or flexible in the event of unexpected outcomes.[616] Such qualities are not in themselves direct expressions of benefit or harm but they become relevant when the prospect of surprise is taken seriously.[617] Likewise, cultivating caution can foster a greater appreciation for properties like diversity: by not putting all the eggs in one basket, so to speak, innovation policy can at the same time mitigate lock-in, hedge against limitations of knowledge, and accommodate divergent interests and values.

---

[606] See paragraphs 4.53 to 4.55.
[607] Fisher L and Harding R (1999) The precautionary principle and administrative constitutionalism: the development of frameworks for applying the precautionary principle, in *Implementing the precautionary principle: perspectives and prospects*, Fisher L, and Harding R (Editors) (Cheltenham: Edward Elgar).
[608] Martuzzi M and Tickner JA (Editors) (2004) *The precautionary principle: protecting public health, the environment and the future of our children*, available at: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.177.1936&rep=rep1&type=pdf.
[609] Fisher E (2007) *Risk regulation and administrative constitutionalism* (Oxford: Hart).
[610] Dreyer M and Renn O (Editors) (2009) *Food safety governance: integrating science, precaution and public involvement* (Berlin: Springer).
[611] Stirling A (2007) Risk, precaution and science: towards a more constructive policy debate *EMBO Reports* **8**: 309-15.
[612] Santillo D, Johnston P and Stringer R (1999) The precautionary principle in practice: a mandate for anticipatory preventative action, in *Protecting public health and the environment: implementing the precautionary principle*, Raffensperger C, and Tickner J (Editors) (Washington, DC: Island Press).
[613] O'Riordan T and Cameron J (Editors) (1994) *Interpreting the precautionary principle* (London: Earthscan).
[614] See Chapter 5.
[615] O'Riordan T, Cameron J and Jordan A (Editors) (2001) *Reinterpreting the precautionary principle* (London: Cameron May).
[616] Collingridge D (1983) Hedging and flexing: two ways of choosing under ignorance *Technological Forecasting and Social Change* **23**: 161-72 and Raffensperger C and Myers N (Editors) (2006) *Precautionary tools for reshaping environmental policy* (Cambridge, Massachusetts: MIT Press).
[617] European Science and Technology Observatory (1999) *On science and precaution in the management of technological risk*, available at: http://ftp.jrc.es/EURdoc/eur19056en.pdf.

8.38 Finally, and most importantly, the virtue of caution involves a respect for the importance of undertaking all these processes under the oversight of a variety of contending social and political perspectives, where these exist.[618] (This relates to the various methods of public participation and inclusive deliberation we have discussed in Chapter 5.)

Reframing surveillance

8.39 The conviction that caution can be exercised simply through attention to issues of risk connects to a second distortion, involving the institutional design of systems of regulation. The concern with issues of risk leads to a temptation to design systems of surveillance and control that seek comprehensively to monitor all relevant activity. This temptation is particularly strong in the wake of panics about the possible consequences of particular innovations[619] and connects to the question of whether and how to manage public perceptions and public reporting of emerging biotechnologies. This overemphasis on surveillance is not a property of emerging biotechnology regulation alone. An overwhelming concern with comprehensive surveillance is virtually a defining character of the regulatory systems that have emerged in the UK in recent decades.[620] It is hardly likely, therefore, that emerging biotechnologies would be an exception to this trend although, in view of our characterisation of the problem posed by emerging biotechnologies, it leaves entirely unexamined the question of whether such measures are either necessary, sufficient or in any way appropriate to meet the objectives of regulation in such contexts.

Reframing command and control

8.40 To those attempting to work with regulation in emerging biotechnologies and, indeed, to the outside observer, the institutional world of biotechnology regulation can look a mess: a complex patchwork of public, private, semi-public, national and supranational institutions and practices with significant duplications and gaps. The temptation to try to rationalise this into something closer to a single system of command and control is very strong, as the widespread resort to command and control as a response to regulatory failures in other domains shows.[621] But setting aside the well known limits to command and control regulation, there is a more pertinent point still: the 'mess' of emerging biotechnologies regulation is a perfectly normal state of affairs in any complex regulatory domain. Attempting to subdue it to a single hierarchical regulatory template, especially one driven by the kind of restrictive understanding of risk described above,[622] is to pursue an illusion.

Reframing regulatory design

8.41 The twin temptations of surveillance and command and control link to a fourth temptation to be avoided. The world of regulatory design is replete with summary prescriptions of how to design regulatory systems to cope with regulatory problems. Some of the most fashionable in recent years have included:

---

[618] European Environment Agency (2001) *Late lessons from early warnings: the precautionary principle 1896-2000*, available at: http://www.eea.europa.eu/publications/environmental_issue_report_2001_22.

[619] See, for example, the generally unfavourable response to GM crops in Europe and the extensive monitoring and control systems associated with GM crops in the European Union. This is an archetypal example and has formed the basis of a significant academic and industrial response to new technologies, wherein relevant stakeholders seek to 'learn lessons' from the GM crop debate during the 1990s, partly with the aim of avoiding such a regulatory outcome. See: Einsiedel EF and Goldenberg L (2004) Dwarfing the social? Nanotechnology lessons from the biotechnology front *Bulletin of Science, Technology & Society* **24**: 28-33; Mehta MD (2004) From biotechnology to nanotechnology: what can we learn from earlier technologies? *Bulletin of Science, Technology & Society* **24**: 34-9. More recent technological developments – such as the nascent DNA sequence synthesis industry – seem to be pushing strongly for self-regulation. See: Schmidt M and Giersch G (2011) DNA synthesis and security, in *DNA microarrays, synthesis and synthetic DNA*, Campbell MJ (Editor) (New York: Nova Science).

[620] See: Moran M (2003) *The British regulatory state: high modernism and hyper-innovation* (Oxford: Oxford University Press).

[621] Such as financial services, following the 2007-8 crash.

[622] See paragraphs 8.7 to 8.8.

- 'smart' regulation (particularly influential in the minds of regulators and policy makers themselves);
- 'reflexive' regulation, denoting regulatory systems especially capable of learning from experience;
- flexible regulation; and
- 'light touch' regulation.

8.42 The extent to which these are just slogans in search of solutions can be seen if we perform a simple mental experiment: trying to imagine anyone designing unintelligent, unreflective, rigid and heavy-handed systems of regulation. A particular temptation lies in the identification of appropriate forms of regulation for emerging biotechnologies with 'soft' regulation.[623] 'Soft' regulation relies heavily on voluntary codes of conduct, on appeals to the sense of moral obligation of the regulated, and on the willingness and capacity of the regulated independently to conform to standards. Its appeals, for example in terms of the level of burden on the regulated, are obvious. In domains characterised by high technical complexity and traditions of professional autonomy (two features important in most areas of biotechnology) in one sense all regulation is 'soft' in that it cannot be conducted without the cooperation of those to whom it applies. However, it would be a mistake to rely on moral obligation and willingness freely to conform as a general principle of regulatory design. Perhaps the most important example of a 'soft' and 'light touch' regulation conducted in the UK in recent years was embodied in the styles and practices governing the regulation of financial markets by the Financial Services Authority before 2007, styles and practices that – to some extent – led to the catastrophe of the financial crisis in the UK and that have produced a pronounced aversion among regulators to the 'soft' mode.[624]

8.43 This is not to suggest that communities engaged in biotechnology innovation are prone to practise the kinds of excesses observed in financial markets. It does suggest, however, that regulatory design is a contingent matter, dependent on particular contextual needs and demands. The design of regulatory institutions, in emerging biotechnologies or elsewhere, offers no magic cure for resolving the 'mess' of the regulatory world inhabited by emerging biotechnologies. The notion of intentional institutional design is, in the words of the political scientist Robert Goodin, a "myth". It is worth quoting his cautionary account: "Typically, there is no single design or designer. There are just lots of localized attempts at partial design cutting across one another, and any sensible scheme for institutional design has to take account of that fact."[625]

8.44 A particularly important recent example of the one-size-fits-all design illusion is provided by the regulatory (or more accurately deregulatory) policies of the Coalition Government that came to power in the UK in 2010. Whatever the arguments in favour of a policy of deregulation generally, the conditions of emerging biotechnology do not support such a single policy line. It is of the very essence of the domain that uncertainty, ambiguity and transformative potential constantly throw up unexpected regulatory challenges. To imagine that these challenges can be met by a single deregulatory rule is illusory. This is not to say that the regulatory future must involve a commitment to regulatory intervention. As we show in the next Chapter, there are instances where regulatory controls can be an obstacle to innovation and commercial exploitation.[626] But any choice, be it regulatory or deregulatory, needs to be contingent on the particular problems raised by any particular technology.

[623] See paragraph 8.31.
[624] See: Financial Services Authority (2009) *The Turner review: a regulatory response to the global financial crisis* available at: http://www.fsa.gov.uk/pubs/other/turner_review.pdf, p86ff.
[625] Goodin RE (1996) Institutions and their design, in *The theory of institutional design* Goodin RE (Editor) (Cambridge: Cambridge University Press), p28.
[626] See paragraph 9.28ff.

Conclusion

8.45 It is rare for there to be a single 'right' regulatory solution, whether the 'problem' to be solved is a substantive regulatory issue or a problem of a feature of regulatory institutional design. That is particularly the case in domains marked, as is emerging biotechnologies, by ambiguity and uncertainty, and it happens also to be a feature, as we have emphasised above, of the nature of design theory in regulation. Regulatory decision making is a special case of a larger feature emphasised throughout this Report, namely, the way decisions constantly close down and open up ranges of options. It therefore follows that what is important in regulation is that, in closing or opening possibilities or choices there has to be, in part, a sense of the *ethical* implications of choices made.

8.46 In one form or other, approaches guided by caution are now embedded in the language of emerging biotechnologies regulation – rightly so, because of those defining features that have loomed large in this Report: uncertainty, ambiguity and transformative potential. However, as is clear from the discussion earlier in this Chapter, the implications of caution are not themselves without ambiguity. This simply adds weight to our advocacy of the virtue of caution: the importance of humility in the face of uncertainty and the importance of considering the widest possible range of affected interests.

8.47 Much of the discussion of public engagement with emerging biotechnologies is couched in the language of 'managing' public expectations and perceptions, particularly expectations and perceptions created and sustained by the mass media. This was noted by a number of those who submitted evidence in response to our open consultation. No doubt the engagement is important for the avoidance of manifestly distorted perceptions. However, there is a more fundamental reason for public engagement and it arises out of a key feature of the regulatory system emphasised throughout this Chapter: the regulation of the domain offers no single, intellectually compelling solutions to pressing regulatory problems. At best it offers only a range of possible solutions, typically involving hard choices between alternatives (hence, dilemmas). The critical features of such choices are that they are, at least in part, ethical in character and have to be made in an uncertain world. Public engagement is not a mechanism for the management of expectation but should be an intrinsic part of the regulatory process albeit that no effective regulatory system can simply consist of a forum for popular choice.

8.48 A key theme of this Chapter has been the problematic contribution of theories of institutional design to the creation of effective regulation. Most regulatory problems are dilemmas. They do not admit of technical administrative solutions but instead involve hard choices that often have significant ethical implications. In emerging biotechnologies, therefore, it is more important to focus on the ethical framework, and the framework of public engagement, than to chase particular forms of institutional design.

Chapter 9

Commercialisation

Chapter 9 - Commercialisation

Chapter overview

In this Chapter we review the challenges faced in commercialising emerging biotechnologies given the peculiarly long development phase and uncertain outcomes associated with them. We review the experience of the pharmaceutical industry (one area to have made significant attempts to commercialise biotechnology) and the way in which all research, including publicly funded academic research, has become dominated by the expectation of future commercial profit.

Since profit in knowledge-intensive industries depends significantly on the existence of a system for the protection of intellectual property, we describe the current system and its limitations as it applies to emerging biotechnologies and find a tendency for patent protection for emerging biotechnologies to be both too broad and too short to provide the commercial incentive it is intended to provide: by being too broad it discourages creative competition and by being too short it does not secure the prospect of sufficient returns on investment. We examine a number of modifications of the patent system or of regulation which address either the problem of excessive breadth or of inadequate length, and find them useful in certain situations.

We make a distinction between different types of biotechnologies and to show the particular problems attached to intellectual property protection in one of them. In particular, for biotechnologies such as pharmaceuticals and plant breeding which involve intervening in existing biological systems we argue that only radical policy changes can deal with the distortion of commercial incentives that result. These build on the foundations of proposals for health impact funds and value based pricing to offer a new way of paying for drugs and new crop varieties based on the value of *impact* on health and agriculture/environment. For other biotechnologies such as biomanufacturing processes, impact payments are unnecessary and inappropriate: here the necessary incentives will be provided by ecotaxation and similar steering of the market mechanism. In both cases there is a role to be played by social engagement to align commercial incentives with public good.

Introduction

9.1 In biotechnology, as in other science-intensive areas, *commercial exploitation* comes only when the conjunctions between relevant knowledge, practices, products and applications are reasonably well developed. We can therefore expect little experience of commercial exploitation in technologies that are only now emerging, where possible conjunctions are still being explored. The most relevant experience we can hope to find will be of the commercial exploitation of the early (and now 'emerged') biotechnologies, for example in agriculture and pharmaceuticals. However, commercialisation might be given another meaning: the infusion of *commercial purpose* into the assembling of that conjunction from the very first and, indeed, the prominence of commercial values in shaping and selecting biotechnologies. In this Chapter we will consider commercialisation in both of these senses. We will argue that emerging biotechnologies now show a great deal of commercialisation in the second sense.[627]

9.2 The set of principles we set out in Chapter 4 relate to choices and decisions that are in some sense political,[628] to which a good deal of time and care can and should be devoted. Commercial activities, on the other hand, operate within the market mechanism. Since Adam Smith, economists have applauded the market mechanism and the profit motive for coordinating the efforts of many people and organisations in taking a multitude of separate decisions (Smith's 'invisible hand') to produce a globally efficient distribution of resource use. It would be naïve to expect that each of these private, individual decisions will always be taken in accordance with the public virtues we identified in Chapter 4. Instead, in this Chapter, we consider what are the regulatory frameworks and institutional forces that affect commercial or commercialised activities involving emerging biotechnologies, and how a public ethics might bear upon these to produce a better alignment of entrepreneurs' decisions with public good than either the market alone or existing public innovation governance can achieve.

9.3 Regarding commercial exploitation, emerging biotechnologies face very different conditions according to sector. The greatest apparent opportunities for profit have been perceived to be in

[627] The implications of market values 'crowding out' other sources of normativity was made emphatically in a recent book by the political philosopher, Michael Sandel; see: Sandel M (2012) *What money can't buy: the moral limits of markets* (London: Allen Lane). Sandel's prescription in response for this situation is a call for a kind of public ethics.

[628] See paragraphs 4.28 to 4.32.

'biopharma', followed by other areas of health care; here, emerging biotechnologies promise to respond to unmet needs and, if they can do so safely, significant commercial returns can be expected. Indeed, some products, such as monoclonal antibodies, are already successfully generating revenue: the most successful of them, adalimumab ('Humira'®)[629] which emerged during the 1990s from Cambridge Antibody Technology's development of phage display technology was, as of February 2012, expected by some analysts to become the highest-selling drug ever over its lifetime, with $7.9 billion of sales worldwide in 2011 alone.[630]

9.4 Biotechnologies have also started to address unmet needs in industrial chemicals and in plant and animal breeding. The main unmet needs in these sectors are reduction of fossil fuel use, and increases in food production within the constraints of existing resources. Here, the public good to be served by these technologies is currently far from being reflected in prices, and therefore profit. Accordingly we have to treat the different sectors separately to a large extent. However, we begin with two relatively common themes that cut across emerging biotechnologies generally: the framing of emerging biotechnologies in terms of commercial values ('commercialisation' in our second sense), and the effect of intellectual property protections.

The profit motive in biotechnology research

Economic rationality and the pursuit of scientific knowledge

9.5 Established businesses are generally wary of investing in emerging biotechnologies due to the probable high cost and delayed, uncertain outcome of commercial exploitation. In the interests of their shareholders they are probably right to be cautious. There are, however, reasons why businesses may diverge from what is in shareholders' interests (understood as maximising their shareholder value). One is the excitement that may be attached to any new technology that offers exceptional potential for profit, especially technologies that are reported by the media to be making a significant profit for other firms. However, for there to be a mania like the dot-com boom of the late 1990s, one other ingredient is required, namely poor returns on capital for low-risk investments. Financiers then have a strong incentive to persuade their clients (and themselves) that the likely returns in new technologies are expected to be higher – and the risk attached lower – than economic history would suggest. The biotechnology boom was not as marked as the dot-com boom, due to the longer time period needed to get products to market but it showed the same cycle of early investment in the 1990s, in the hope of high returns, followed by disillusion after 2000 when the difficulties became more apparent.[631] Such 'biotech mania' has now subsided.

9.6 The other deviation from economic rationality arises from the inclinations of those who work in the private sector. High quality scientists are needed by businesses in order to develop marketable and saleable products, but such scientists are likely to be interested in 'the science itself' rather than merely sales, profits and incomes. The private sector therefore must accept that some of its employees working in research and development (R&D) will be keen to put their time and energies into advancing research rather than focusing solely on advancing firms' profits. In fact JK Galbraith's concept of the 'technostructure'[632] makes a similar point about whole body of higher-level employees. In the managerial capitalism which developed in large firms in the 1930s and 1940s, such employees collectively freed themselves to a large extent

[629] Adalimumab is used to treat a number of illnesses, including Crohn's disease, several types of arthritis and psoriasis.
[630] Comer B (2012) Brand of the year: Humira *PharmExec* February 1, available at: http://www.pharmexec.com/pharmexec/article/articleDetail.jsp?id=757392.
[631] A significant sobering moment was the death of Jesse Gelsinger, the first recorded person to die in a gene therapy clinical trial. See: Wilson JM (2009) A history lesson for stem cells *Science* **324**: 727-8. See also Lähteenmäki R and Lawrence S (2007) Public biotech 2006 – the numbers *Nature Biotechnology* **25**: 729-37, for detail on biotechnology financing in the very early years of this century.
[632] Galbraith JK (2007) *The new industrial state* (Princeton, New Jersey: Princeton University Press).

from the close control of shareholders, and could indulge their interest in the growth and survival of their firm as opposed to its profitability.

9.7 Clearly, under managerial capitalism the sectional interest of scientists in carrying out research is more likely to be indulged than under a managerial approach that prioritises profit. During the 1980s a counter-revolution began in the US and the UK to reassert the maximisation of shareholder value as the goal of management. As growth requires profit and profit requires growth, the change is not necessarily obvious. The managerial approach depends on shareholders' understanding of how profit can be made: a venture capitalist may be as motivated by profit as an asset-stripper, but the former aims to make profit through investment in technology, the latter does not. Long-term commercial funding *may* be available for R&D of biotechnologies that are expected to give a good commercial return. Modest funding may also be available for R&D that is not expected to generate large profits, especially where large firms have subscribed to the values of corporate social responsibility. In general, however, the climate requires R&D programmes to carry a realistic prospect of profitability.

Research and profit-seeking in the pharmaceutical sector

9.8 As we have seen, biotechnology can be used in a wide range of sectors, but until now the bulk of research and commercial exploitation has been in health care in general and research-intensive pharmaceuticals.[633]

9.9 Shareholders, naturally, want research to generate profit. The motives of scientists in drug discovery are generally more complex. For example, they may have left academic research in order to get their research funded rather than to enrich themselves financially. Nonetheless, Big Pharmaceutical Firms (BPFs) have been using stock options to motivate senior R&D personnel by aligning their interests with those of shareholders. Some BPFs have recently introduced a system of bonuses for R&D personnel based on the delivery of new drugs to the next stage of the pipeline. Perhaps the most extreme reorganisation is that at GlaxoSmithKline (GSK) where small business units, analogous to in-house biotechnology firms, have to compete with one another for funding, and get it only as long as their projects are successful.[634]

9.10 Shareholder value now appears to demand drastic reductions in the research carried out by in-house R&D in corporations, in favour of increased dependence on university and similar research, packaged in spin-outs. The consensus among BPFs is now to let the dedicated biotechnology firms (DBFs: largely university and industry spin-outs) do much of the most speculative and creative research, such as studying the pathway of disease and working out how to counteract it, as well as carrying out pre-clinical testing of the new active substance (NAS[635]) they produce. At this point, it is possible that a BPF may be prepared to invest in the NAS. One mechanism for the provision of funds is that, when a pre-arranged milestone is reached, sufficient funding is made available for the next stage of the research. The more funds the BPF provides, the larger its stake in the drug. Alternatively, there may be a trade sale of the whole DBF to the BPF. Rarely, an independent DBF may wait until its NAS is ready for market and then licence it to a BPF (if at all).

9.11 Whatever happens to the outputs of the spin-out, there is one inevitable consequence of its existence: those university scientists involved in it will do their scientific work with an eye to the

[633] I.e. non-generic pharmaceuticals.

[634] See, for example, evidence given by Dr Ian Tomlinson, Senior Vice-President - Head of Worldwide Business Development and Biopharmaceuticals R&D at GlaxoSmithKline, to the House of Commons Select Committee on Science and Technology: "Innovation comes from one person having an idea, or a small group having an idea, and prosecuting that idea to some kind of milestone. That is why we have changed dramatically over the last five years. We used to have thousands of people working in R&D. We would throw a load of people at the problem and we would hope to solve it in that way. Now, we have 50-people groups, with a leader fully empowered to prosecute a very specific area of science. If they work, great. If it does not work, that is Darwinian evolution. You have a model where people are accountable for prosecuting a specific area of science." House of Commons Science and Technology Committee (2012) *Bridging the "valley of death": improving the commercialisation of research*, available at: http://www.publications.parliament.uk/pa/cm201012/cmselect/cmsctech/uc1936-i/uc193601.htm.

[635] This term is used in preference to new chemical entities (NCEs) to encompass large molecule drugs (e.g. monoclonal antibodies) as well as small molecules that were the traditional targets of pharmaceutical firms.

profit that it may yield, as will colleagues who may consider following their example. In this they are likely to be encouraged by senior colleagues and managers within the university, since the institution will have a share in the equity and will be able to charge for the use of university facilities (to say nothing of impact studies in the Research Excellence Framework[636]).

9.12 What we have described are the elements of a transformation: 20 to 30 years ago, in pharmaceuticals, the field comprised mainly curiosity-driven scientists in universities and research institutes cooperating with (and partly funded by) scientists in corporate research laboratories, who themselves had licence to 'think long'. Now the latter are driven hard to generate profit and the former are also very interested in it. In other sectors of biotechnology, such as industrial biotechnology, the present situation is similar, with the difference that, in newly emerging industries, there is no corporate golden age to look back to and rather less scope for a DBF to sell to a big firm. Given the importance of profit to the commercial sectors in which biotechnologies are exploited, to understand the market's effect on the social shaping of biotechnologies we must focus squarely on how profit is made in biotechnology, and how far the profit made reflects the value of biotechnology to society.

Patent protection for public goods

9.13 A central activity, for both commercial and non-commercial biotechnology research, is the production of knowledge. Knowledge of any kind is usually considered to be a public good in the weak sense that it is *non-rivalrous* in use but it may also exhibit the characteristic of being *non-excludable*.[637] As such, in emerging biotechnologies as elsewhere, much of the organised generation of scientific knowledge is funded by Government and, in the case of biomedical research, by charities too, because it is assumed that it will be underprovided by commercial organisations who cannot secure sufficient profit from it. It is in this sense that, for example, the Biotechnology and Biological Sciences Research Council refers to 'public-good plant breeding'.[638] (Of course, scientific knowledge may come about as a by-product of commercially-funded research, or indeed through the experience of using technologies, or experimentation with them. The emphasis on academically organised scientific research, in fact, may lead us to neglect the contribution of these other activities both to the fund of scientific knowledge, which may then be taken up as a bridge to further knowledge, and to human welfare more generally.)

9.14 In order to encourage the commercial development of knowledge, enforceable patents or other forms of intellectual property rights (IPR) have been used as a way of making the knowledge generated by research an excludable good. Patenting knowledge also makes it possible for profit to be made from the use or licensing of that knowledge. The nature and effects of IPR are central to the commercialisation of biotechnology, and therefore to this Chapter. In the next section we therefore set out the framework of IPR as they apply to biotechnologies in general and emerging biotechnologies in particular. With those clear, we shall proceed to the problems that arise in ensuring adequate incentives for the commercial development and use of emerging biotechnologies.

---

[636] The Research Excellence Framework is the system for assessing the quality of research in UK higher education institutions; assessments against this framework are used by funding bodies to inform the allocation of funding to institutions; see: http://www.ref.ac.uk. See also paragraph 6.38ff.

[637] See paragraph 4.6ff.

[638] See for example, BBSRC (2004) *Review of BBSRC-funded research relevant to crop science*, available at: http://www.bbsrc.ac.uk/web/FILES/Reviews/0404_crop_science.pdf, p6. The BBSRC noted to us: "The BBSRC does not have a standing definition of 'public-good'; instead we work with a shared understanding of its meaning. Public-good research will often address needs that are not currently being met by market-forces. In the context of the crop science review, "public good" refers to (pre-) breeding related work on traits not necessarily of immediate interest to commercial breeders but which would be needed in the longer term to address societal concerns about climate change etc., so called sustainability traits e.g. stress tolerance, resource-use efficiency etc. It is important that there is some benefit to the public and that the research is not solely to the advantage of any specific commercial entity." BBSRC, personal communication, 6 September 2011.

Purpose and operation of the patent system

9.15 The purpose of the patent system, as recently set out by Lord Neuberger in the UK Supreme Court, is

> "…to provide a temporary monopoly as an incentive to innovation, while at the same time facilitating the early dissemination of any such innovation through an early application for a patent, and its subsequent publication. Although this is true in any sector, it has particular force in the pharmaceutical field, where even many of those who are sceptical about the value of intellectual property rights accept that there is a public interest in, and a commercial need for, patent protection."[639]

9.16 The subject matter of the case in which this statement was made was, in fact, a biotechnology product, specifically a therapeutic monoclonal antibody. However, when the patent was applied for, the drug had not yet been made, let alone had its safety and efficacy established. The patent covered the production of this antibody by a gene sequence that the patentee had discovered and that, owing to its similarity to known gene sequences, they believed would be the code for proteins that had a predicted physiological effect. The controversy concerned an issue where emerging biotechnologies present a particular challenge to the patent system: what should be the scope of patent protection for a technology whose *potential* is uncertain? Here the lower courts had, in effect, held the patent to be too speculative validly to cover the monoclonal antibody; the Supreme Court, however, disagreed.[640]

9.17 Patent applications are published within 18 months of their filing or priority date (the date used to establish novelty/obviousness),[641] but cannot be enforced unless and until they are granted. A granted patent confers a monopoly that endures for 20 years from filing of the patent application,[642] although where the patent protects a new drug or agrochemical this can, in the EU and US and some other jurisdictions, be extended to up to 25 years to take account of delay in securing regulatory approval. Patents provide a monopoly over the subject matter of the patent claims in the terms in which they were granted.[643] Unlicensed operation within the scope of such claims exposes those responsible for it to the risk of an award of damages and an injunction against continuing infringement. However, the monopoly conferred by the claims of a granted patent is not absolute; thus, throughout Europe it is not an infringement of a patent to operate within the scope of the claims where this is done for the purposes of research into the claimed invention, even where this is done commercially or for commercial purposes.[644] However, where the patent claims are sufficiently broad to cover any innovation that results

---

[639] *Human Genome Sciences Inc v Ely Lilly & Co* [2011] UKSC 51, available at: http://www.supremecourt.gov.uk/decided-cases/docs/UKSC_2010_0047_Judgment.pdf, paragraph 99.

[640] A Technical Board of Appeal of the European Patent Office also came to a similar conclusion as the Supreme Court. See: European Patent Office (21 October 2009) *T 0018/09 (Neutrokine/Human Genome Sciences)*, available at: http://www.epo.org/law-practice/case-law-appeals/recent/t090018eu1.html.

[641] See: IPO (2012) *After you apply*, available at: http://www.ipo.gov.uk/types/patent/p-applying/p-after.htm.

[642] See: Intellectual Property Office (2012) *What is a patent?*, available at: http://www.ipo.gov.uk/types/patent/p-about/p-whatis.htm. In fact, this may be up to 21 years after the very first filing of a patent application if this very first filing is treated as a claim only to priority.

[643] Patent claims as granted are almost invariably narrower, and often *much* narrower, than the claims in the patent application as filed. Much ill-informed and alarmist comment about patents is based on the claims in the application as filed (e.g. in the case of synthetic biology, the patent applications dating from 2005 filed on behalf of Synthetic Genomics Inc. and its associates) when in practice it can often take several years for a patent to be granted, whereupon its true protective scope becomes apparent. There is thus an element of uncertainty in the process, but because a search report identifying relevant prior art is also published at the same time as the patent application it should usually be possible to make an informed assessment as to the likely scope of any patents that might be granted as a result of the application.

[644] The precise expression is "experimental purposes relating to the subject matter of the invention." See: IPO (2008) *The patent research exception: a consultation*, available at: http://www.ipo.gov.uk/consult-patresearch.pdf, p8. Thus, it does not apply to the use of a patented technology as a tool for experimenting on something else. This 'research tool'" issue has given rise to some expressed concerns, notably in academic research settings but there is no evidence that it has thereby restricted research. Much confusion has arisen from the fact that there is no corresponding defence in the US, although the 'Bolar' defence overlaps with it to the extent that the research in issue is directed towards a new therapeutic or diagnostic that will require regulatory approval; see: Cook T (2006) *A European perspective as to the extent to which experimental use, and certain other, defences to patent infringement, apply to differing types of research*, available at: http://www.ipeg.com/_UPLOAD%20BLOG/Experimental%20Use%20for%20IPI%20Chapters%201%20to%209%20Final.pdf.

from that research, they provide a potential barrier to the subsequent commercialisation of such an innovation.[645]

Other relevant kinds of intellectual property protection

Trade secrets

9.18 Patents are one of three main forms of intellectual property protection encountered in biotechnology. In contrast to patents, trade secrets can be protected for so long as they remain confidential, which they would not be once a patent application disclosing the secret is published. Trade secrets can confer effective longer term protection on technology that cannot be reverse engineered from products that are placed on the market, such as technology relating to processes. Fermentation conditions are an example of such process knowledge in biotechnology but the range of possibilities is not wide; this is probably for the best, because secrecy detracts from wider dissemination of the innovation. Trade secrets have a further failing as compared to patents as although most national patent laws provide for "prior user" rights so that someone who can prove that they were secretly using a process that is subsequently patented by a third party can continue to use such process without infringing the third party's patent, their "prior user" rights tend to be narrow in scope in that they do not allow for use in another jurisdiction and often do not cover improvements in the process.

Regulatory data protection

9.19 The third form of intellectual property protection encountered in biotechnology is regulatory data protection: data concerning the safety and efficacy of regulated products such as drugs and agrochemicals as submitted to regulatory bodies is protected for a fixed term against the regulatory authorities cross referring to it for the purposes of granting regulatory approvals to second applicants.[646] Protecting regulatory data clearly provides an incentive to undertake the safety and efficacy studies needed to bring new drugs to market; otherwise second applicants could 'free ride' on the enormous investment in such studies.[647]

Marketing exclusivity

9.20 Yet further forms of protection that offer a targeted incentive exist in biotechnology, such as the marketing exclusivity conferred in the EU and the US on orphan drugs.[648] This gives the first firm to secure regulatory approval for a drug that treats a rare disease a true exclusivity for a number of years as against another person securing a regulatory approval for the same or a similar drug for the same indication, even where the latter has generated a full data package of

[645] Again, however, the barrier is not absolute, even absent voluntary licensing. This is because throughout Europe the owner of a "dependent patent" that represents an improvement over an earlier "dominant patent" can seek a compulsory licence, although this is in practice rarely done, in part because a separate application for such a licence must be made in each European country. In the US, which lacks a statutory compulsory licensing regime, a similar result is achieved in practice because the Supreme Court has held that the grant of an injunction against a patent infringer is not automatic: *eBay Inc. v. MercExchange, L.L.C.,* 547 U.S. 388 (2006), available at: http://www.supremecourt.gov/opinions/05pdf/05-130.pdf.

[646] Although, like patents, the protection of such regulatory data is internationally mandated by virtue of the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), it is much less specific as to how this is to be done than it is for patents, and so for example, unlike patents, does not specify any minimum term. The term differs as between jurisdictions and according to the nature of the regulatory framework and the type of substance being protected. In Europe it is now ten years for the first medicinal product to contain a new active substance, extendable for one further year only if approval of important new indications is secured. See: European Medicines Agency (2012) *European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure*, available at: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004069.pdf , paragraph 35.1.1.

[647] As it is, the term of regulatory data protection is usually keyed to the first authorisation for a particular active substance, so the system does not adequately protect the investment in later studies into new indications.

[648] Ten years in the EU and seven years in the US. See: European Medicines Agency (2012) *Orphan incentives*, available at: http://www.emea.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000393.jsp&mid=WC0b01ac0580024c5a and s.527 Federal Food, Drug, And Cosmetic Act [21 USC 360cc], respectively.

their own.[649] This recognises that patents and regulatory data protection alone are inadequate to provide an incentive for research into some rare diseases, as the possible economic return will be too low.

Limitations of intellectual property for emerging biotechnologies

9.21 Trade secrecy, as we note above,[650] has little obvious relevance to emerging biotechnologies. The same is true of regulatory data protection and marketing exclusivities, since these require a suitable regulatory framework. By their nature, emerging biotechnologies, particularly those that are manifested, at least in their early stages, as enabling technologies[651] rather than specific products, often lack such a well adapted framework.[652]

9.22 This leaves patents as the most important form of intellectual property with the potential to protect emerging biotechnologies.[653] However, for emerging biotechnologies, patents suffer from two main inadequacies. Firstly, their term is likely to be *too short* to recoup investment in the patented subject matter: much, if not all, of the 20 year patent term for those patent applications filed in the early stages of emerging biotechnologies is likely to have been consumed by the time that the technology is commercialised.[654] Secondly, such patents risk, much more than in better developed areas of technology, being *overbroad*. This second tendency may result in patents having a potentially chilling effect on third parties bringing products or processes to market that are within the scope of such patent claims, for so long as the patents remain in effect. Not that research on their subject matter necessarily constitutes infringement,[655] but the commercialisation of its results may require a licence. This, in turn, is likely to have an adverse effect on research directed to such products or processes.

9.23 Patent systems find new types of technology much more of a challenge than existing ones. There are two main reasons. The first is that, institutionally, patent offices that examine patent applications and determine the scope of claims to grant can only effectively do so against a background of relevant prior art. However, in the early years of an emerging biotechnology the most relevant prior art will be in various different areas of technology.[656] This means that relevant prior art may more easily be overlooked and there is thus an even greater risk than usual that patents may be granted with claims that cover, or are obvious in the light of, prior art. Such patents can be challenged in subsequent court proceedings but this is costly and therefore rare. The more they exist in any technical field, the greater the potential chilling effect on third parties looking to commercialise the products of their own research.

---

[649] Thus it can protect, in a way in which regulatory data protection does not, investment into later studies into new indications, such as stratified treatments for common complex diseases where the treatment is based, say, on a rare genotype.

[650] See paragraph 9.18.

[651] Patents for enabling technologies can be more difficult to monetise than patents that cover specific products, although there are some exceptions, such as the Cohen-Boyer patent on recombinant DNA technology (US 4237224, available at: http://www.google.com/patents/US4237224) and the suite of patents, originally held by Cetus, on various aspects of the polymerase chain reaction. See, generally, Beardsley T (1984) Biotechnology: Cohen-Boyer patent finally confirmed *Nature* **311**: 3 and Rabinow P (1997) *Making PCR: a story of biotechnology* (Chicago, Illinois: University of Chicago Press).

[652] See paragraph 8.26.

[653] Some commentators challenge from an economic perspective the value of patents in many sectors but still conclude that patents have value to the certain sectors; see, from the perspective of US patent law: Bessen J and Meurer MJ (2008) *Patent failure: how judges, bureaucrats, and lawyers put innovators at risk* (Princeton, New Jersey: Princeton University Press), arguing that from an economic perspective the patent system works substantially best in the chemical and pharmaceutical industries and noting that, despite problems in biotechnology patenting with early stage inventions, patents are probably most important to biotechnology start-ups.

[654] The earliest patents in the field of nanotechnology date from around 1991 and have now expired. The basic patents in RNA interference (RNAi) date from around 2001 and so have less than ten years still to run but as yet no commercial product based on RNAi technology has been authorised. Lundin P (2011) Is silence still golden? Mapping the RNAi patent landscape *Nature Biotechnology* **29**: 493-7.

[655] See footnote 644.

[656] In recognition of this problem the USPTO created in 2004 (nearly 15 years after the earliest patents for it had been filed) patent class 977, dedicated solely to nanotechnology. Class 977 is a secondary classification, which means that patents in that class are also classified in accordance with the more traditional technology to which they relate. For more information on class 977 patents, see: USPTO (2012) *Class 977 nanotechnology cross-reference art collection*, available at: http://www.uspto.gov/patents/resources/classification/class_977_nanotechnology_cross-ref_art_collection.jsp.

9.24 The second difficulty with new technology arises from the fact that patents inevitably include a degree of speculation: the claims as ultimately granted cover not only what the patentee has actually shown to work but also what can, in the light of that demonstration and the state of the art generally, also be expected to work. These ought not, however, to be so broad as to exclude the prospect of non-infringing alternatives that might be commercialised. The judgment as to what degree of speculation is appropriate for coverage by a patent claim, which defines the scope of the patent,[657] is not easy at the best of times; however, it is much more difficult with an entirely new type of technology. This problem is not a new one: the following principle as articulated in the US Supreme Court in 1966 is still apt, in Europe as well as the US, today:

> "This is not to say that … we are blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public. *But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."* [658]

9.25 However the problem is not always readily addressed, as can be seen from the monoclonal antibody case mentioned above.[659] Excessive breadth of patenting is more likely in new fields. But in a new field there is a further danger, that some early patents cover developments that provide the foundations for future inventors and innovators. If those developments are, in effect, unavailable to all but the patent holder, inventive and innovative activity beyond mere research will be severely restricted.

9.26 These various shortcomings are difficult to address, partly because they are to some degree in conflict. As a consequence, in the context of emerging biotechnologies, there is likely to be a combination of what might be an overly short term of protection with the risk of overly broad protection during that short term. We see below that this must limit the sort of commercial support that emerging biotechnologies can attract.

9.27 Short duration may be particularly troublesome for pharmaceuticals, because of the delays forced by the regulatory system; on the other hand, patent duration can be extended for pharmaceutical products from the basic 20 years up to 25 to compensate for this. What longer patent duration cannot compensate for, in pharmaceuticals, is the extra cost of meeting requirements for regulatory approval (such as clinical trials), the additional delay this represents before getting a return on the money already spent, and the possibility that approval will be denied.

The economics of the 'patenting problem'

9.28 In paragraphs 9.15 to 9.17 we examined patenting problems for emerging biotechnologies from a legal perspective. Now we apply economic analysis to show that, in some key areas of emerging biotechnologies, there are other formidable problems which can be expected not only to reduce the rate of investment but to move it away from realising the social value of biotechnologies.

9.29 We have seen that knowledge is intrinsically a non-rivalrous good but can be made excludable by patenting or other IPR. This exclusion allows the market mechanism to apply to the production of knowledge; but the market mechanism can never work really efficiently because of the non-rivalrous aspect. In other words, the necessary incentive for commercial production of knowledge is based on charging for its use (a royalty or a profit margin on top of the cost of producing a medicine or other product) when the use of knowledge in fact incurs no direct cost

---

[657] For a discussion of patent claim scope from an economic perspective see: Merges RP and Nelson RR (1990) On the complex economics of patent scope *Columbia Law Review* **90**: 839-916.

[658] *Brenner v. Manson* 383 U.S. 519 (1996), available at: http://supreme.justia.com/cases/federal/us/383/519/case.html. (Emphasis added).

[659] See paragraphs 9.15 to 9.16.

to anyone.[660] So, if a medicine costs 20 cents per dose to produce and distribute but is sold for $2 per dose (in order to pay for the R&D cost of developing it plus trying to develop many other drugs that failed during development), many of those patients who would get it if it were priced at 20 cents per dose, and benefit from it, will not get it. This represents a loss to them and to society overall.

9.30 This restriction of use is a failure of the market mechanism, but it is not the only one. Arguably a worse market failure is that many drugs (and other fruits of knowledge) which should have been developed will not be developed at all. Let us examine with some care what this means. If we knew costs and benefits in advance, we could say that a drug *should* be developed if the cost of development, and any other necessary fixed cost, is less than the net benefit to society that will come from its use. Here we must also recognise that the returns needed to keep pharmaceutical firms at work developing new drugs must include covering the costs not only of developing the drugs that they bring to market but also of the R&D that goes into the large number of those that they do not, that is, those drugs that were abandoned for some reason during development (for example, because of problems with scaling up production, unfavourable clinical trials or a poor financial forecast). In practice there are great uncertainties and most drugs selected for development will fail, but experience suggests that the following scenario is plausibly close to a possible reality for a particular therapeutic area.

- Out of ten drugs chosen for development, nine will fail, costing a total of $900m in R&D spending written off.
- One succeeds, costing $200m to develop. It will be sold for $2 per dose (profit margin over variable costs, $1.80) and, in total (before the patent expires), will sell 500 million doses over its lifetime. It will then make a profit over variable costs of $0.9 billion.
- By itself it then looks like a successful project. But the total development cost of the one successful and nine failing drugs will be $1.1billion, leading to a loss of $0.2 billion.[661] It would then not be in shareholders' interests to proceed with this programme, if such an outcome could be expected.[662]

9.31 Looking at the issue from the point of view of society as a whole, should those ten drugs, the successes and the failures, have been developed? The answer will, very probably, be that they should, because we should take into account not only the producer surplus (i.e. profit) over variable cost, which we calculated at $0.9 billion, but also two blocks of consumer surplus: the difference between what consumers had to pay (or what was paid on their behalf), and what the drug would have been worth to them. The first block of surplus is that for the patients who would get the drug at $2 per dose; the second is that for the extra patients who would have got the drug had it been charged at variable cost of 20 cents per dose. Adding that to the $0.9bn might well have taken the total surplus over the $1.1bn mark.

Innovators versus 'me-toos'

9.32 It is typical in pharmaceuticals that a radically innovative new product will be followed by so-called 'me-toos'. Thus, in drug development, the first NAS to address a particular pathway of disease and therapy – the first statin, say, for cardiovascular therapy, or (in recent biopharma) the first monoclonal antibody which is a beta-lymphocyte stimulator – will be followed by others, developed by rival firms. The early followers may well be would-be radical innovators who lost

[660] Of course, many conditions may need to be satisfied to allow the knowledge to be used, that incur costs and are not necessarily of a generic nature, such as the costs of infrastructure and the cost of training personnel to be able to use the knowledge. These 'sunk' costs account for the immobility of capital even where returns are low, relative to other possible investments, or even negative.

[661] The example is hypothetical but not unrealistic. The generally quoted figure for the cost of developing a drug to the point marketing is $802 million (in 2000-value dollars), which also takes account of the cost of failures. DiMasi JA, Hansen RW and Grabowski HG (2003) The price of innovation: new estimates of drug development costs *Journal of Health Economics* **22**: 151-86.

[662] We have ignored the marketing costs, because they are neither fixed nor an absolutely necessary variable cost. Taking them into account will clearly make the financial outturn even worse. We return to these costs later, at paragraph 9.64.

the race to be first to market; the real me-too drugs, however, are those whose development was initiated in response to the arrival of the innovator. In some cases a me-too drug will turn out to be squarely better than the innovator's; in other cases different drugs will best suit different groups of patients; in others again, the innovative drug will be as good as it gets, and the me-toos will serve no purpose. In all cases, the later comers will get some, probably substantial, share of the market. In one sense this is as it should be: patients will be either better treated, or at least not worse, than if the innovator kept a monopoly.

9.33 Where me-toos are damaging is in what they do to the incentive to innovate, for example, to produce the first statin or beta-lymphocyte stimulator. The innovator, and those rivals who tried to innovate but lost the race, must share the profits to be had from their successful gamble – their commitment of large R&D funding to projects which could be expected to fail – with others who waited until many of the uncertainties had been resolved. Even less of the social value from the innovation will accrue to the innovator; there is even less incentive to fight through the R&D and regulatory jungle, making a path for others to follow.

Intellectual property rights as encountered in emerging biotechnology

9.34 The argument so far has been a general one, but indexed to the specific case of pharmaceuticals. We need therefore to consider how widely it may be applied. At this point we need to make a distinction between three types of biotechnologies:

1 those that are intended to affect biological systems in their natural context (relatively open systems like the environment or relatively closed systems like individual patients receiving medical treatment);
2 those that utilise biological processes or systems in a controlled context to produce outputs for other purposes (e.g. engineered biofuels, bioreactors); and
3 those that provide knowledge or information about biological processes or systems (like gene sequencing or stem cells used in toxicology).

9.35 The two main 'type 1' sectors, (bio)pharmaceuticals and plant breeding, are similar in that there is a separation between the research-intensive firms that innovate and produce patentable knowledge, and the multitude of doctors and farmers who manage the interface with the biological systems (human bodies and agriculture) without, in most cases, doing any formal R&D themselves.[663] This concentration of research upstream, and the risks attached to the letting loose of drugs and new plant varieties in those biological systems, means that an exceptionally high proportion of cost is accounted for by R&D and other fixed costs, and therefore the price of any product that emerges needs to be far above variable costs.[664]

9.36 Another specific feature of the pharmaceutical sector is its exceptional degree of dependence on patents and IPR more generally. The 'me-too problem' largely arises from this: published patents produce a target for inventing round and once that is achieved, it is relatively easy to break into the market that the original innovator has established. The me-too problem may be general in 'type 1', since the original innovator demonstrates with the NAS (or other new product developed) how to intervene in a biological system, and other firms may then follow. We saw this for pharmaceuticals, where the system is human bodies, and the situation seems similar in crop plant breeding, where the system is agricultural.

[663] Of course the development of techniques and biotechnology tools brings some research into the context of use or treatment, for example developing patient-specific genetic tests in clinical conditions. One vision of synthetic biology is of a kind of 'bricolage' by which users can design biological products to address specific needs as they encounter them.
[664] We shall see below that this is at least as true for biopharma as for 'chemopharma'.

9.37 'Type 2' – essentially biomanufacturing[665] – involves a different type of knowledge and learning process, since the core of the task is to manage a closed system. A bioreactor, for example, is a manufacturing plant and so the business of R&D into more advanced bioreactors is bound up with the business of manufacturing. The lead innovator (in the *processes* of the bioreactor) establishes a lead manufacturing capability through its R&D. It then learns by doing (which economises on R&D spend) and may well thereby increase its lead. The task for the follower is more difficult than for the pharmaceutical firm developing a me-too drug. The first mover advantage is greater, because of the learning by doing, and less dependent on IPR – more on secrecy and other assets. This is probably also the case for 'type 3'. Certainly the case of Oxford Nanopore (see Box 9.1) suggests that gene sequencing is free of most of the problems which beset pharmaceuticals.

Box 9.1: Oxford Nanopore

Early attempts at gene sequencing by imaging a single molecule with a scanning probe microscope have proved unsuccessful so far. However, another approach, in which the bases are read out as single molecules of DNA are threaded through a nanoscale pore, has generated significant momentum since the method was first proposed in 1996.[666] This is currently the subject of a significant commercialisation effort by firms such as Oxford Nanopore, exploiting the pore-forming proteins that were introduced as biosensors.[667]

Oxford Nanopore is a UK firm that was set up in 2005 to commercialise this technology. It has been fully funded by "long-term [British] investors".[668] It brought its first product to market in 2012, a product which (if the commentary is to be believed) is a sure-fire commercial success because it offers greater speed for lower cost in a market that has been already developed by others. This product faced few, if any, regulatory barriers. If we suppose that at least some of its patents were filed after 2002, it would have at least ten years of patent-protected production, without allowance for follow-up patents. The apparently smooth translation of scientific knowledge into technology with a broad range of applications, combined with the absence of high regulatory barriers (owing to the fact the product does not directly utilise or impact on biological systems), provide a stark contrast to the experience of firms such as those in the pharmaceutical, biomedical or agricultural biotechnology sectors developing biological or biologically active products.

9.38 We conclude that the market failure in patenting that we are discussing is concentrated in type 1 activities. This failure is important not because (and certainly not only because) it leaves commercial potential unexploited but primarily because of the social value represented by the foregone consumer surplus. Pharmaceuticals and plant breeding differ, of course: thus the regulatory protection of human bodies from damage by drugs is more elaborate – and therefore more expensive for the innovator – than that protecting ecosystems from damage by new varieties of plant (or animal). This may help to account for social resistance (in Europe) to transgenic plant varieties. The result is at least as expensive for the would-be innovator as the requirement for elaborate clinical trials.

9.39 Another variation between pharmaceuticals and plant breeding is in the extent and effectiveness of IPR protection in developing countries. Until recently it was pharmaceuticals whose protection was weaker – indeed non-existent – in many developing countries because (where patents were recognised at all) product patent protection for pharmaceuticals was specifically excluded. Now the general acceptance by developing countries of TRIPS includes pharmaceutical product patents. Meanwhile the development of new plant varieties, largely transgenic, which breed true, makes plant breeders more dependent on IPR than before.[669] While it will usually be possible to identify and pursue pharmaceutical firms in developing countries that produce a patented drug without a licence, to take on a multitude of individual farmers who have transgressed, each using crops grown their own fields, would be a formidable undertaking (see Box 9.2).

---

[665] For a discussion of biomanufacturing, see: Morgan S, Colon S, Emerson JA *et al*. (2003) *Biomanufacturing: a state of the technology review*, available at: http://www.che.ncsu.edu/academics/concentrations/documents/Biomanufacturing-AStateofTechRev.pdf.

[666] See: Kasianowicz JJ, Brandin E, Branton D and Deamer DW (1996) Characterization of individual polynucleotide molecules using a membrane channel *Proceedings of the National Academy of Sciences* **93**: 13770-3.

[667] See: Braha O, Walker B, Cheley S *et al.* (1997) Designed protein pores as components for biosensors *Chemistry & Biology* **4**: 497-505.

[668] Cookson C (2012) Oxford Nanopore unveils mini-DNA reader *Financial Times* 16 February, available at: http://www.ft.com/cms/s/2/318a378a-5900-11e1-b118-00144feabdc0.html#axzz252CYKeNP.

[669] Conventionally, seed merchants supply F1 hybrids which do not breed true – that is if the farmer plants seed from the crop it is much less productive than the original seed supplied.

Box 9.2: The limits of patent protection in a global context

We suggested above that intellectual property held in developed countries may obstruct research in less developed ones. However, there is also an opposite risk in such countries, that intellectual property will be ignored altogether. The case of Bt cotton in India offers a striking example. The cotton plant had been engineered to contain a bacterial transgene (from *Bacillus thuringiensis*) for the production of a toxin lethal to a small number of different kinds of insect larvae. Despite opposition from activists concerned about genetically modified (GM) crops, farmers wishing to avoid the costs and dangers of using pesticides were keen to obtain seeds. Seeds disappeared from the test plots that were established in 2002 under authorisation from the Indian Government. By 2005, it was estimated that 2.5 million hectares were under 'unofficial' Bt cotton (twice the area of authorised plantings).[670]

> "The unofficial Bt cotton varieties had been bred, either by firms operating in an ambiguous legal position or by farmers themselves. A veritable cottage industry had sprung up, a state described as 'anarcho-capitalism', whereby small-scale breeders were crossing reliable local varieties with the caterpillar-proof Bt plant…. The world's first GM landraces had arrived, a blend of tradition and science..."[671]

We would not hazard a view on the legality of what the Indian farmers did. At all events, if it had been illegal, we suppose that many would have done it nonetheless, and that the firm that developed the new varieties would have had no success in getting royalties from those who thus used its innovation at one removed.[672] However, the consequence of unchecked 'anarcho-capitalism' of this sort is very likely to be a reduction of the incentive to invent and innovate further technologies that may hold significant and even transformative potential, and, once the ambiguities (highly evident in this case) are worked through, potentially transformative in genuinely beneficial ways for less developed countries.

9.40 'Type 2' emerging biotechnologies suffer from a quite different kind of market failure: the under-pricing of carbon and other environmental 'goods' and 'bads' in relation to their social impact (particularly long term impacts), which should make their competitors considerably less competitive than they in fact are. As systems of industrial production, 'type 2' emerging biotechnologies are mostly in competition with other systems of industrial production, notably those employed in synthetic chemistry. Their key advantage in this competition is their economy in the use of natural resources, particularly energy. The lower their products are priced, the less that advantage tells.

9.41 Plant breeding is also affected by this market failure, but in a subtler manner. A plant might be genetically engineered to thrive when drenched in every kind of fertiliser and pesticide, and irrigated (Variety A); or it might be genetically engineered to do remarkably well in the absence of fertiliser and pesticide, and irrigation (Variety B). So while the bioreactor is squarely *discouraged* by environmental under-pricing, plant breeding is merely *distorted* by it: towards Variety A and away from Variety B. (We see no strong effect of environmental under-pricing on either pharma or 'Type 3' biotechnologies.)

Crossing the 'valley of death'

9.42 In this Chapter we have reviewed the operation of the patent system with regard to emerging biotechnologies, and we have found it does not contribute favourably to the rapid and profitable commercial exploitation of emerging biotechnologies, most notably in pharmaceuticals. The problem of translation, of moving drugs from bench to bedside, has become known as the 'valley of death' at least since the Cooksey report in 2006.[673] While many promising NASs are

[670] Kingsbury N (2009) *Hybrid: the history and science of plant breeding* (Chicago, Illinois: University of Chicago Press), p417.
[671] Ibid.
[672] Where Monsanto does have valid patents, as in North America, it has sued farmers for infringement where the farmers say their seed has been contaminated by patented Monsanto seed grown nearby. For one discussion of a case where a farmer was found to have infringed Monsanto's patents, see: Fox JL (2001) Canadian farmer found guilty of Monsanto canola patent infringement *Nature Biotechnology* **19**: 396-7. Monsanto itself has been sued for "compensatory damages for revenues lost through contamination of organic crops with the companies' GM herbicide-tolerant canola". See: Bouchie A (2002) Organic farmers sue GMO producers *Nature Biotechnology* **20**: 210. For Monsanto's position statement on the matter, see: Monsanto (2012) *Why does Monsanto sue farmers who save seeds?*, available at: http://www.monsanto.com/newsviews/Pages/why-does-monsanto-sue-farmers-who-save-seeds.aspx.
[673] For the Cooksey Report, see: Cooksey D (2006) *A review of UK health research funding*, available at: http://webarchive.nationalarchives.gov.uk/+/http:/www.hm-treasury.gov.uk/d/pbr06_cooksey_final_report_636.pdf. The term 'valley of death' does not appear in the Report itself but "Bridging the 'valley of death'" is the rubric for an inquiry by the UK House of Commons Science & Technology Select Committee which began in December 2011. See: House of Commons

discovered and studied by biotechnology firms, it is a general complaint heard from all sides that there is a gap between the point that biopharmaceutical research can get to on the basis of the public sector grants available, and the point at which the uncertainties have been reduced enough for a BPF to buy in, in the way described at paragraph 9.10.

9.43 This matters, very obviously, not because of the welfare of drug firms and their shareholders, but because of the well being of patients that might be improved: again, the question of opportunity cost must be considered at the broadest level. It is possible, in principle, for venture capital to bridge this gap but it is hard and/or unacceptable in practice, because venture capitalists demand a very large stake in return for their investment. There may be specific reasons for the limitations of venture capital in the UK,[674] but the problem is clearly worldwide.[675] The exorbitant terms of venture capital funding arise from their perception of risk (which depends on their understanding of the technology and the market).[676]

9.44 In the next section we shall examine remedies proposed (some of which are already implemented) for the obstacles to commercialisation discussed above.

Remedies for patenting problems

9.45 There are, in principle, at least two ways of avoiding the dampening effect of excessively broad patents on further invention in a field. One is compulsory licensing, whereby all who wish to use the patented process or make the patented product, may do so in return for payment of a royalty, the level of which would be determined by some kind of regulator. Such systems exist,[677] but they are little used, perhaps because they cost as much as challenging the validity or scope of a patent. That might be altered but to do so risks reducing the incentive and reward to the inventor.

9.46 A second way to avoid the restriction is to avoid patenting in the first place through open access and pre-competitive research. The classic example of the avoidance of patenting is the open source movement in software, revolving around Linux.[678] (Open source licensing in software nevertheless remains dependent on an underpinning of intellectual property, namely copyright, as without this there would be nothing to license.) It is parts-based approaches to synthetic biology that offer the closest case in emerging biotechnologies to computer software. These approaches aim to develop a suite of modules that have been standardised for assembly into products that have characteristics which can be reliably predicted from the nature of their components, allowing rational design of biological systems. To the extent that this can be achieved it will open up the possibility of innovative behaviour to almost everyone who can order components online, akin to software programming in the 1980s.[679] One option is that biological parts, processes and information should circulate in common, so to speak, but could also be

Science and Technology Committee (2012) *Bridging the "valley of death": improving the commercialisation of research*, available at: http://www.publications.parliament.uk/pa/cm201012/cmselect/cmsctech/uc1936-i/uc193601.htm.

674 Smith G, Akram MS, Redpath K and Bains W (2009) Wasting cash – the decline of the British biotech sector *Nature Biotechnology* **27**: 531-7.

675 See, for example: Ernst & Young (14 June 2011) *Despite renewed growth in 2010, biotech industry faces R&D challenges*, available at: https://webforms.ey.com/GL/en/Newsroom/News-releases/Beyond-borders_global-biotechnology-report-2011.

676 Certainly venture capitalists, looking for some scope for an early exit from a project in which they invest, will be much more interested in funding research that is close to market and that can at least identify a tangible end product that can be brought to market whilst there is still a respectably long period of intellectual property protection for it. Venture capitalists do however favour investing in firms that have already filed patent applications and these firms will do better than those that have not. See: Cao JX and Hsu P (2010) *Patent signaling, entrepreneurial performance, and venture capital financing*, available at: http://efmaefm.org/0EFMSYMPOSIUM/Toronto-2011/papers/Hsu.pdf.

677 See, for example, the World Trade Organization's Doha declaration. The declaration allows member states to grant compulsory licences for patented drugs during a public health crisis. World Trade Organization (20 November 2001) *Declaration on the TRIPS agreement and public health*, available at: http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm.

678 For contrasting views of progress with open source software, see 'Babbage' (2012) Difference engine: free is too expensive *The Economist* 30 March, available at: http://www.economist.com/blogs/babbage/2012/03/desktop-linux; 'Monitor' (2012) An open-source robo-surgeon *The Economist* 3 March, available at: http://www.economist.com/node/21548489.

679 See: Thambisetty S (2012) *The analytical significance of emergence in the patent system*, available at: www.nuffieldbiothics.org/emerging-biotechnologies-evidence-reviews, p29.

used privately and for exclusionary purposes.[680] An example of such hybrid openness is the 'BioBrick'® public agreement.[681] It can be argued that this combination is an ideal arrangement for commercial organisations, which can 'piggy-back' on advances made by others and then protect their own innovations. One attraction of openness of this kind is that it need not exclude researchers and users in less developed countries, who might otherwise face a 'patent blockade' constructed by firms and others in developed countries. This is not to say that the scientists who have espoused open source in synthetic biology would necessarily accept such a compromise.

9.47 Another means to the same general end is to designate certain areas of research as pre-competitive. There is much current discussion[682] regarding collaborative research as a way of increasing productivity, and such a designation would be an enabling move for this. The idea is that results from research designated as pre-competitive would be placed in the public domain from the start, being disseminated via the internet and published in learned journals, rather than patented. This would then advance the status of the field as a whole and allow the protagonists to compete with one another from a more advanced starting point, increasing the overall chances of success.

The problems of uncertainty and excessive time to market

9.48 In paragraph 9.27, we note that for all pharmaceutical firms the insistence on rigorous and exhaustive clinical trials not only increases the total cost of R&D but, by delaying the point at which the drug can reach the market, reduces the time it can be sold under patent. In any new area like biopharma and, more particularly, emerging biopharma, unexpected difficulties are likely to make for further delays, as well as increasing the uncertainty (poison to venture capitalists and other prospective funders) as to whether the drug will ever be successful. Drug discovery in pharmaceutical and biotechnology firms is a particular case in point where two problems reduce the probability of success and extend the period from patent application to launch: firstly, the lack of truly validated therapeutic targets and secondly, the lack of surrogate endpoints or biomarkers that are accepted by the regulators.

Validated therapeutic targets

9.49 Many drugs fail in the clinical evaluation stage because the predictions of animal experiments carried out early in the discovery process are not realised in human patients. Moreover, experimental medicine studies on human volunteers do not predict the efficacy or lack of efficacy of a treatment in patients. Coupled with this, it has been noted that between 70 and 80 per cent of therapeutic targets are shared across the industry (perhaps not surprising given that medical need is the driver for all the research projects in the first place) so that working together to validate models for some or all of these targets would be mutually beneficial. The amount of information available to work with is increasing exponentially owing to the accumulation of relevant biodata (particularly genomic data) and there is increasing recognition that most diseases need to be approached by studying a network of genes rather than by looking for the effects of a single gene that are disease related.[683] This argues in favour of sharing data and the formation of consortia.

9.50 A number of firms are now making information about problems they wish to solve public via the internet (so called 'crowdsourcing') and may give grants to institutions or individuals who

[680] Ibid, p35.
[681] See: BioBricks Foundation (2012) *The BioBrick™ Public Agreement (BPA)*, available at: http://biobricks.org/bpa.
[682] See, for example, Norman TC, Bountra C, Edwards AM, Yamamoto KR and Friend SH (2011) Leveraging crowdsourcing to facilitate the discovery of new medicines *Science Translational Medicine* **3**: 88mr1.
[683] Chen Y, Zhu J, Lum PY *et al.* (2008) Variations in DNA elucidate molecular networks that cause disease *Nature* **452**: 429-35; Schadt EE (2009) Molecular networks as sensors and drivers of common human diseases *Nature* **461**: 218-23.

express a wish to work on a potential solution but without claiming the intellectual property at this stage.[684]

Box 9.3: Crowdsourcing therapeutic targets

Some pharmaceutical firms have placed information in the public domain in the hope that it will kick-start research by academic groups that will help validate the targets. For example, the release into the public domain by GlaxoSmithKline of 13,000 structures of potential anti-malarial drugs.[685] In other cases it has been achieved by forming public private partnerships (PPP) such as Arch2POCM.[686] The objective of this PPP is to demonstrate in a phase II clinical trial that the mechanism of the selected disease target can be safely and usefully modulated. The consortium includes US, EU and Canadian regulators, pharmaceutical firms, academic institutions, patient advocacy groups and contract research organisations and all data generated will be made public without any patent claims being made.

Surrogate endpoints

9.51 Increasingly, it is necessary to perform pivotal studies in many thousands of patients to get the necessary safety and efficacy data to obtain marketing authorisation for a NAS with a novel mechanism of action. One way of shortening the path to market is to establish a reliable surrogate marker that the regulatory authorities will accept as evidence of efficacy, for example, lowering low-density lipoprotein cholesterol in plasma. Once accepted, the biomarker facilitates the activities of all those wishing to produce drugs in the same therapeutic class. This approach is probably best demonstrated in the cancer field and has already led to a personalised medicine approach for some therapeutic targets.[687] The discovery of biomarkers is approachable through collaborative processes in the same way outlined above for validation of drug targets and may be an integral part of the activity in some cases.[688]

Commercialisation and social value

9.52 All the proposals discussed above may well encourage the commercialisation of emerging biotechnologies, and in the appropriate situations, where they correct or compensate for failings of the patent system, we would support their use. More general actions by Government may also encourage commercialisation, such as the 'patent box' initiative, which guarantees firms a reduction on corporation tax (up to ten per cent) on all profits attributed to qualifying patents.[689] However, the patent system itself, while it endures, remains relatively inflexible, allowing the innovator to obtain all the profit they can for a predetermined period, followed by open competition in which prices are expected to fall towards the marginal cost of production. According to our analysis, this means the social value of innovation is likely to be restricted in the short term and relatively well exploited in the longer term, which is not necessarily an optimum profile (albeit that it coincidentally imposes a gradual and cautious approach to introduction of new products by initially restricting use through affordability). However, our main concern is not to find ways of getting more commercialisation of emerging biotechnologies but to get better commercialisation – to connect it more closely to social value.

9.53 Corporate social responsibility may play a role as a form of soft regulation (discussed in Chapter 8), giving a firm's products a 'soft value' to partners and consumers in addition to their hard economic value, and steering their commercial activities towards socially valuable (or less harmful) outcomes. While there is dispute about whether visible and earnest corporate responsibility may have a positive effect on firms' profits in the long term or compromise the efficiency of markets, standards of corporate social responsibility do provide opportunities for consideration of how innovative measures and technologies may increase sustainability and

[684] Lessl M, Bryans JS, Richards D and Asadullah K (2011) Crowd sourcing in drug discovery *Nature Reviews Drug Discovery* **10**: 241-2.
[685] Cressey D (2011) Traditional drug-discovery model ripe for reform *Nature* **471**: 17-8.
[686] Norman TC, Bountra C, Edwards AM, Yamamoto KR and Friend SH (2011) Leveraging crowdsourcing to facilitate the discovery of new medicines *Science Translational Medicine* **3**: 88mr1.
[687] Million RP (2006) Impact of genetic diagnostics on drug development strategy *Nature Reviews Drug Discovery* **5**: 459-62.
[688] See paragraph 9.49.
[689] See: Intellectual Property Office (2012) *How to use the 'Patent Box' regime to cut your corporation tax*, available at: http://www.ipo.gov.uk/news/newsletters/ipinsight/ipinsight-201207/ipinsight-201207-3.htm.

ameliorate social impact.[690] Despite the limitations of corporate social responsibility information as a form of soft regulation, we believe that the corporate social responsibility movement represents an important way of bringing social values into commercial activities. We therefore recommend that **innovation should be included in corporate social responsibility reports as a separate, specific issue**.

9.54 There may be, however, more direct ways in which to connect innovation with social value. In the next section we focus on proposals squarely designed with this objective. One of these proposals is significantly new.

Intellectual property rights and incentives: addressing the fundamental problems

9.55 The commercial exploitation of biotechnology, in pharmaceuticals and elsewhere, depends heavily on the legal protection of intellectual property. We argued above that there are fundamental difficulties in using a system of intellectual property rights to provide the right incentives for commercial organisations to produce and use new knowledge. It is clear that these problems are all the more acute where technologies are new. We have considered some possible – and actual – modifications of the system to address some of these problems. These show some promise, in particular, in addressing the way over-broad patenting may obstruct the work of subsequent innovators, and in drawing a useful line between, on one hand, scientific and cooperative commercial advance (in the early stages of discovery) and, on the other, the later stages, where it is every firm for itself and patent protection is vital. But the two fundamental problems remain: that patent protection of knowledge restricts its commercial use, and that the market situation to which it leads creates a pattern of incentives and rewards that matches the social value of innovations rather poorly. This situation is indeed becoming less favourable to innovation, in pharmaceuticals at least: the rivals of innovating firms are becoming more efficient at developing me-too drugs, and health organisations under pressure to contain costs are turning at the earliest opportunity to generic alternatives. While this may have short term advantages (more cheap drugs, more quickly) it will not support the long term health of the industry which is necessary if that industry is to be the global engine of therapeutic advance.

9.56 A solution to the problem of the divergence between social value and market value may lie in creating conditions in which the reward for innovation better corresponds to the social value of that innovation. This may be perhaps rather obvious in principle although it is likely to be very challenging in practice, since it involves evaluating the comparative social value of the use of a product and rewarding innovation separately from the price paid for the product. Nevertheless there are conditions in some sectors of biotechnology, and might be in others, that could support such an approach. We therefore recommend that **consideration should be given to state interventions in the market for new biotechnologies to secure the social benefits of innovation through direct reward for socially valued innovations**.

Reflecting the social value of innovation

9.57 It happens that in pharmaceuticals, the UK Government has been something of an innovator in finding an alternative to the simple market mechanism to place a value of certain technologies. The UK's National Institute for Health and Clinical Excellence (NICE) has the responsibility of assessing the therapeutic value of new drugs, in terms such as quality-adjusted life years (QALYs) gained by the patient, and deciding whether (given the price that is proposed) the use of a given drug in the National Health Service (NHS) would be cost-effective, taking into account the drugs and treatments already available, and their prices. The NHS can avoid the use of

[690] For example, ISO 26000 on social responsibility; in common with many standards of private and public 'full cost accounting', contains references to the use of innovative technologies to address social concerns and increase sustainability, although this is currently guidance rather than certifiable standards. See: International Organization for Standardization (2010) *ISO 26000 project overview*, available at: http://www.iso.org/iso/iso_26000_project_overview.pdf.

drugs that are over-priced in relation to their comparative clinical value, and the firm introducing a new drug has an incentive to keep the price below the level that might lead to an adverse judgment by NICE. With an advanced apparatus in place to assess the value of new drugs, the UK Government now plans to go one stage further, and introduce a system of value-based pricing, in which the prices for branded pharmaceuticals that firms are permitted to charge to organisations within the NHS will be worked out on the basis of their value, the assessment of which will involve consideration of "the range of factors through which medicines deliver benefits for patients and society".[691]

9.58 These advances have one fundamental limitation: the price paid for a drug will have to go on performing two functions: to compensate and reward the innovator for the cost and risk they have taken to bring the drug to market, and to guide the user. A new biopharmaceutical product may very well give a big gain in QALYs to one category of patients, a modest gain to another category, and in total be something of a niche product. In that case the first function demands a very high price; however, given the increasing pressures for cost control within the NHS (and all health systems), that price may deny the drug to patients who would have benefited from its prescription. Very simply, "for medicines to be widely accessible, prices need to be low, but low prices do not encourage innovation."[692]

9.59 What is needed, then, is to disconnect the two functions. The clinician should use the drug if its value to the patient exceeds the cost of producing and distributing it, which is usually very modest. The price would need therefore to be set at around that modest level. The compensation and reward to the innovating firm should reflect the social value of its use, which may be high. Clearly it will not get that from the price, so it must receive some kind of supplementary payment. Again this is not a new idea in itself but it has been put forward in a very specific and limited context.[693] However, there are reasons to think that the limitations of such a specific scheme in that context need not apply generally or, pertinently, in the UK.[694]

The idea of a health impact fund

9.60 Under the scheme, a 'Health Impact Fund' (HIF) would be set up to reward pharmaceutical firms that develop drugs mainly for use in developing countries:

> "All pharmaceutical firms worldwide would have the option of registering new medicines with the HIF. By registering, a firm agrees to provide its medicine at a price near the cost of production anywhere it is needed. In exchange, the company will be paid by the HIF annually for 10 years based on the fund's assessment of the actual global health impact of the medicine as a proportion of the global health impact achieved by all products registered with the HIF."[695]

9.61 The HIF proposal has been considered by the World Health Organization (WHO), and the judgment of a Consultative Expert Working Group has been expressed in a recent WHO Report;

---

[691] Department of Health (2010) *A new value-based approach to the pricing of branded medicines: a consultation*, available at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_122793.pdf.

[692] WHO (2012) *Research and development to meet health needs in developing countries: strengthening global financing and coordination – report of the consultative expert working group on research and development: financing and coordination*, available at: http://www.who.int/phi/CEWG_Report_5_April_2012.pdf, p161.

[693] The proposal is set out in Hollis A and Pogge T (2008) *The Health Impact Fund: making new medicines accessible for all*, available at: http://healthimpactfund.org/hif_book.pdf, with more detail in Incentives for Global Health (2011) *Health impact fund*, available at: http://www.who.int/phi/news/phi_7_cewg_hif_submission_jun2011_en.pdf. A critique of the proposal can be found in Sonderholm J (2010) A reform proposal in need of reform: a critique of Thomas Pogge's proposal for how to incentivize research and development of essential drugs *Public Health Ethics* **3**: 167-77.

[694] The WHO rejected the HIF proposal, largely on the basis of practical difficulties in implementation, in particular, in establishing a measure of health impact in the context of developing countries (see: WHO (2012) *Research and development to meet health needs in developing countries: strengthening global financing and coordination – report of the consultative expert working group on research and development: financing and coordination*, available at: http://www.who.int/phi/CEWG_Report_5_April_2012.pdf.) However the development of QALYs by NICE and the plans for value-based pricing already address many of these substantial difficulties, and the centralised structure of the NHS offers an unusually favourable context for such a scheme. If it will work anywhere, it is likely to work in the UK.

[695] World Health Organization (2012) *Consultative expert working group on research and development: financing and coordination*, available at: http://apps.who.int/gb/ebwha/pdf_files/WHA65/A65_24-en.pdf, p150.

after conceding a number of merits in the proposal, the Working Group rejected the proposal in view of practical difficulties in its implementation, in particular, in establishing a measure of health impact in the context of developing countries.[696]

9.62 This criticism is certainly telling, but mainly for developing countries. Since the avowed aim of the HIF is to benefit developing countries, and that was the concern of the Working Group, there was no discussion of its applicability to developed countries. However, with the development of NICE and the plans for value-based pricing,[697] much of the assessment apparatus already exists in the UK, or is being developed. Furthermore, given the centralised structure of the NHS, the circumstances prevailing in the UK appear unusually favourable for getting 'a sufficiently reliable measurement of health impact'.

9.63 As in the proposal for developing countries, so for the UK it would make sense to make participation voluntary, at least in the first instance. The payment rules could be similar: 'based on the… assessment of the actual… health impact of the medicine as a proportion of the… health impact achieved by all products registered with the [UK] HIF.' The total UK HIF moneys to be thus divided up would need to be large enough to ensure that genuinely innovative drugs yielded more profit than they would have done if they had been subjected to the ordinary pricing system (by then, presumably a 'value-based' system). The aim might be ultimately to move to the health impact system – low base pricing plus health impact payment (HIP) – across the board.

Impact on marketing costs

9.64 It is interesting to consider what such a system would do to the marketing activities of innovating firms. (The marketing expenditures of research-intensive big pharmaceutical firms are typically comparable to their R&D spends.[698]) The unethical (and illegal) promotion of off-label prescribing[699] would be simply irrational in this system, assuming that the monitoring system recorded these prescriptions as negative value to patients and therefore reduced the health impact payment accordingly. Once all drugs were subject to the health impact (HI) system, there would be much less to gain from encouraging doctors to prescribe, say, one firm's beta-lymphocyte stimulator rather than another's. The overall payment pot for beta-lymphocyte stimulators as a whole would be maximised by each patient getting the right one for him or her, and for beta-lymphocyte stimulators being prescribed not as widely as possible, but as widely as desirable. According to how the HI system were established, the beta-lymphocyte innovator(s) could get the bulk of the HI payments for this drug class, regardless of the pattern of sales, and me-too followers would get little payment.[700] The total marketing spend of pharmaceutical firms would clearly fall substantially, to public benefit.

---

[696] WHO (2012) *Research and development to meet health needs in developing countries: strengthening global financing and coordination – report of the consultative expert working group on research and development: financing and coordination*, available at: http://www.who.int/phi/CEWG_Report_5_April_2012.pdf, p57.

[697] See paragraph 9.57.

[698] A recent study found that pharmaceutical firms spent "almost twice" on promotional expenditures what they spent on R&D, in the US. (Gagnon MA and Lexchin J (2008) The cost of pushing pills: a new estimate of pharmaceutical promotion expenditures in the United States *PLoS Medicine* **5**: e1). This study includes as 'promotional' a number of expenditures often excluded: notably promotional meetings and phase IV 'seeding' trials. However, it excludes necessary expenditures on packaging and distribution, which are normally included in 'marketing' expenditure. Given the high prices charged for drugs on the US market, it is reasonable to suppose that promotional expenditures are exceptionally high there, thus our rather cautious judgment.

[699] For example, GlaxoSmithKline (GSK) allegedly promoted its anti-depressant 'Paxil'® to US doctors to use for the treatment of children, when it had not been approved for their use. GSK settled out of court for $3bn, for this and a number of other charges. Economist editorial (2012) The settlers: American prosecutors wring $3 billion from GlaxoSmithKline *The Economist* 7 July, available at: http://www.economist.com/node/21558313.

[700] Of course this would depend on performance, and would not apply when a me-too drug dominated the market due to superior outcomes.

The health impact system and the social shaping of emerging biotechnologies

9.65 Throughout this Report, we have argued that emerging biotechnologies should not, individually, be constrained or favoured but that technological development should, in general, be shaped and steered in the direction of public good by conditions that express a public ethics. A system that rewards innovators for the social value of innovation separately from the market cost of production provides an opportunity for public discourse to contribute to the shaping and steering. True, the most obvious influences will be those of three groups of experts. There will be, as there already are, those in firms who decide which drugs to develop and go on developing; and those in regulatory bodies who decide whether to approve the drugs submitted to them. There will also be a third group who have to work out what the outcomes were of the use of particular drugs or other therapies. However, this third group need not completely control the *valuation* of the outcomes; that can partly be done beforehand. This aspect of valuation is one in which public ethics could and should play a role.

9.66 This valuation might also reflect the judgment that excellent low-tech alternatives to advanced drugs are available; for example, specific and feasible lifestyle changes that might not only cut down the rate of new cases, but go a long way to controlling the condition, perhaps in many cases reversing it. In such a case it might be decided, in comparing the outcomes of new drug treatments with the best previously available alternatives (BPAA), that lifestyle changes be included in the BPAA; pharmaceutical firms might well conclude that there is more money to be made from developing therapies for the many conditions that, on present knowledge, cannot be controlled or reversed by lifestyle changes, or even (to a large extent) prevented. It seems to us that the judgment about what should be treated as part of the best available alternatives to new drugs is one in which public ethics could and should play a role.

The internationalisation of health impact payments

9.67 At paragraphs 9.59 to 9.63, we argued that if a HIP system would work anywhere, it would work in the UK, and that the UK, therefore is an ideal place to start. But if it works in the UK then, in the end, it could work anywhere. Just as it would pay the UK to be a pioneer, because there would be gains in the efficiency of use of drugs, so it would pay other countries with reasonably centralised health systems to follow, possibly saving on the initial cost of the assessment system because that had already been developed. And as one developed country after another joined in, the incentives to firms for innovative drug development of high social value would increase. The better established the HI assessment system, the easier it would be to extend it to at least *some* developing countries, and thus to open the road to the original concept of the HIF.

Impact payments beyond pharma

9.68 Our 'impact' argument has focused on pharmaceuticals thus far because, firstly, the problems we are addressing are much the more pronounced in 'type 1' emerging biotechnologies and, secondly, the impact payment system needs to be managed by a monopoly purchaser, or a state which is able and willing to regulate an industry with large numbers of consumers – for which prices can be set centrally and monitored on a sampling basis. This applies to pharmaceuticals and other medical products but it could also apply to plant breeding. In plant breeding the importance of developing countries is arguably greater. It might well be agreed that plant breeding for developing countries, given climate change and scarcity of (for example) water, deserves a Crop Impact Fund on the lines of the HIF, as originally proposed: a fund financed by aid money and/or carbon credits, which would reward innovative plant breeders (whatever the technology used) according to the social value of the plant variety introduced into developing countries. It would be relatively easy to use satellite photography followed by sampling on the ground to establish the extent to which a new variety of crop plant was used; this would then need to be combined with studies of the agronomic and ecological impact.

9.69 In general, the opposition to transgenic crop varieties is based on predictions of small benefit and large adverse consequences: for example, that farmers will become more dependent on plant breeding firms and on chemicals such as herbicides supplied by them, while not gaining the promised increases in yields. If a plant-breeding firm accepted that it would profit from its investment (if at all) on the basis of (neutral) impact assessment, this opposition might well be

moderated. As with health impact, there is no reason why lay people should not participate in valuing agricultural and ecological impact. The lay people who distrust GM crops might agree with the technologists who enthuse over them to put a high social value on reduction of the need for fertilisers and eutrophication.[701] On the other hand, the impact payments might be reduced where evidence was available that low-technology alternatives (inter-planting with leguminous plants, for example) were available.

Incentivising 'type 2' emerging biotechnologies

9.70 In paragraphs 9.37 to 9.40, we note that 'type 2' biotechnologies appear to face quite different problems in commercialisation from biopharma: general discouragement due to 'environmental under-pricing'. In this case we can express social value in the simplest way: by getting rid of under-pricing through eco-taxation or the equivalent use of 'permits to pollute'. Where a given chemical can be produced either synthetically or in a bioreactor, the relative cost of the latter process will fall. Where, for example, biotechnology produces micro-organisms which can greatly cheapen the production of ethanol from cellulose residues, or of biogas from sewage,[702] a carbon tax will make the biofuel resulting still more competitive with fossil fuels. On the other hand, these expectations may be derailed by hidden complexities or intractabilities. As with an impact payment scheme it is not necessary to know or to take a view on the likelihood of different outcomes, although managers and financiers of biotech firms must do so. If their micro-organism fails, they lose the money they invested. What is necessary is that any firm that makes such an advance should know that it will earn more than would now be the case.

Conclusion

9.71 The goods that biotechnology creates are essentially public goods; paradoxically, emerging biotechnologies are infused with commercial values from the very beginning, from the political stakes placed on the growth prospects of the knowledge economy (as we saw in Chapter 7)[703] to the personal interests of researchers (as we saw in Chapter 6)[704] and the entrepreneurial interests of firms with R&D capacity. (Military and charitable biotechnology development are, for different reasons, less infused with commercialism, although they, too, must interact with commercial contexts.) However, as a dominant tool for the allocation of resources, the market mechanism is poor at meeting social demand for these goods or at generating goods that meet social demand. From an investment perspective, the discourse of high ambition that initially made biotechnologies attractive appears to have fallen victim to the characteristic uncertainties that we identified in Chapter 3. As investors find less uncertain opportunities for investment, those who are institutionally committed to biotechnology – such as pharmaceutical firms – struggle to find business models that make economic sense.

9.72 Nevertheless, the unmet need remains for the benefits that proponents of biotechnology claim it will be able to deliver. The problem is that mechanisms intended to protect market incentives to produce them, principally IPRs, do not function efficiently either to guarantee sufficient reward to innovators or to foster the innovative efforts of competitors. The market value of biotechnology and its social value (or potential market and social values) diverge. We have therefore considered the principle, and one possible practical approach, to separating the reward for innovation from the price paid for products, that is, separating the public goods in which the main value of biotechnologies is invested from the private goods that give them physical form. The reason for putting such a principle into practice would be, in cases in which markets may fail to maximise the social value of innovation, to move away from a situation in which market values determine innovation in biotechnologies towards one in which social values do so. This involves the determination of the social value of biotechnologies through the kind of public

[701] The impact on the ecosystem of response to abnormal levels of artificially introduced nutrients or other substances, for example, bloom of phytoplankton in water or reduction in oxygen levels in the sea impacting on fish populations.
[702] Nuffield Council on Bioethics (2011) *Biofuels: ethical issues*, available at: http://www.nuffieldbioethics.org/biofuels-0.
[703] See paragraph 7.10ff.
[704] See paragraph 6.49ff.

discourse ethics we developed in Chapter 4. The aim in doing so is to restore the proper relationships between markets and society, with markets as tools for distributing resources rather than autonomous forces dictating social organisation and the possible forms that social relations may take: in this sense market determinism is just as corrosive to common social life as the technological determinism discussed in Chapter 4.

Chapter 10

Conclusions: emerging biotechnologies and the public good

Chapter 10 - Conclusions: emerging biotechnologies and the public good

Introduction

10.1 The broad nature of our brief has meant that our treatment of the ethical and social issues surrounding emerging biotechnologies is necessarily quite general. We have forsworn consideration of 'case studies', trying always to stand back from particular contexts in order to see emerging biotechnologies as part of a bigger picture, one that engages our attitudes towards science and technology as responses to social challenges and as forces shaping social relations and material well-being. Our subject has not been emerging biotechnologies but how we think about emerging biotechnologies, and how this thinking affects and is affected by what biotechnologies emerge. We have therefore ranged widely across intellectual disciplines and explored diverse literatures as our enquiry has demanded. This has produced some unexpected juxtapositions.

10.2 Our own approach is deliberately interdisciplinary – as we observed early on, finding the terms of an unbiased and open engagement between different values and interests within different normative frames is the proper subject of an 'ethics' of emerging biotechnology governance.[705] This frame always has to be constructed – it is not already there, waiting to be discovered by a process of abstract reasoning.

10.3 In this Report, we began by observing the diversity of our subject matter, that there are almost no features shared in common between biotechnologies. Indeed, because (although not only because) they often come about through the convergence of existing technologies of different kinds, there may be more variation among biotechnologies than between a given biotechnology and non-biological technology. Nevertheless, although we could not clearly define them as a class, we found a way of addressing emerging biotechnologies, as the assembling of knowledges, practices, products and applications, that involved significant 'biological' elements. In order to do this we had to refocus our attention on the nature of 'emerging' as a process rather than the nature of the biotechnologies that emerge. This led us to identify uncertainty, ambiguity and transformative potential as important features that mark out emerging biotechnologies, and which constitute the problem with which research, policy and commerce must engage.

Our argument for a 'public ethics'

10.4 Before drawing together our conclusions we now summarise the main steps in the argument that we have developed in the course of this Report.

a) Biotechnologies have the capacity to produce public benefits but also public harms, both direct and indirect, possibly in ways that are transformative (i.e. that transform the horizon of future possibilities, for example, by locking in dependency on particular technologies, perhaps even ones not yet invented). This may involve a deferral of responsibility for tackling the challenges we presently face to a future in which it is assumed more powerful solutions will be available (the 'biotechnology wager').

b) There is a public interest both in the fact that new biotechnologies emerge and in *which* biotechnologies emerge because (1) they hold potential for benefit and harm (so we want the beneficial ones) and (2) there are always opportunity costs (there are better and worse technologies so we want the *most* beneficial ones; in any case it is unlikely that we can have all of them so some selection is inevitable).

[705] See paragraph 4.42 above.

c) This public interest in having beneficial biotechnologies entails that there should be public support for generating as many prospects for achieving this as possible – the commercial sector should not and cannot do this alone. But the public interest is in achieving socially beneficial ends, so their achievement through technology is merely contingent: the options for achieving those ends may be broader than simply new or 'high' technology.

d) In debates about technology options the concepts of 'benefit', 'harm', 'better', 'poorer', etc., are ambiguous and the nature and likelihoods of different outcomes arising from biotechnologies uncertain, and frequently contested. Although the discourse on biotechnology is saturated with claims about public benefits in terms of economic and social impacts, and this is encouraged by competition for research funding, these claims are difficult to examine and too rarely interrogated.

e) Instead, ambiguities tend to be decided by the way in which biotechnology choices are *framed* and uncertainties smoothed over by promissory narratives that significantly play down the complexity and difficulty of realising the imagined benefits. (For example, we observe that policy decisions are often framed by the privileged concept of economic growth, which dominates other types of values, and articulated within models of innovation that downplay real-world contingency.)

f) This may lead to policy that is both ethically and strategically flawed: *ethically* flawed because to favour particular kinds of response to social objectives on the basis of a limited range of values may actually detract from the optimisation of overall social value; *strategically* flawed because attempts to control the innovation system may actually fail to optimise the benefits explicitly sought.

g) Rather than pursuing pathways defined in advance by technical elites, or leaving it to the market to produce and select economically successful products (or some hybrid of these) emergence of biotechnologies should be continuously shaped by the environmental conditions of the research and innovation system. And these conditions should not be determined piecemeal but should be established by engagement between diverse interests under terms that orientate them towards the public good. There is a need to cultivate procedural and institutional virtues that encourage this and operational mechanisms to enable it.

Our conclusions and recommendations

10.5 Early on in the Report, in Chapter 1, we described the choice of technological trajectories as a process that was subject to significant historical contingency. The technological solutions to human problems that are chosen are not the only ones possible, and may, indeed, not always be the 'best' ones. The solution to human and social challenges is seldom a choice between a given technology and nothing, but more usually between a variety of technological and non-technological – or, more likely, mixed – possibilities. The fact that a given technology may appear to be the best or only path available may be a result of the 'problem' to which it is a 'solution' being framed as a technical problem looking for a technological solution of a certain type. Conversely, it may be a result of undue attention being given to a particular technology so that 'its' range of problems appear more pressing or important than another range of problems that do not have such a solution. We observed that the possible pathways for a range of options cannot always be seen clearly in advance, especially where certain preferred technological pathways are assumed to be urgent and without alternatives. We therefore recommended a more circumspect approach in which **commitments to particular technological pathways should be evaluated not only in terms of their expected future impacts but also by comparison to possible alternative pathways; this can help to illuminate obscured assumptions, constraints and mechanisms of the innovation system, and help to identify sites and opportunities for more constructive governance, prioritisation and control** [paragraph 1.18]. This is not to oppose technological innovation, since the alternatives might be other technologies; rather it is to adopt a questioning approach to dominant ways of thinking about technology that we believe may be entrenched by untested or outdated assumptions.

10.6 The approach that we propose as a way of putting this into practice in the context of biotechnology research, development and innovation is the 'public discourse ethics' that we develop and describe in Chapter 4. This is intended to give public decision making a properly public orientation by opening up the framing of decisions to the full range of understandings and values that are relevant to them. As we say, the task of public discourse ethics is finding the terms of an unbiased and open engagement between relevant positions and interests, so that it is not captured by particular interests or interpretive frames.

10.7 One important procedural measure through which the virtues of public discourse ethics may be expressed is 'public engagement'. Of course the engagement itself can already be framed by certain influential interests, and so the procedure needs to be able to open up the questions to alternative framings. We conclude that there is no single 'best' method of public engagement and that the choice of approaches will always involve dilemmas.

10.8 Public engagement cannot, however, replace the responsibility that attaches to properly vested and accountable authority, and it should not therefore be constrained by the need to reach unambiguous conclusions. Indeed, the attempt to do so can lead to overstepping its inherent conditionality in the same way that expert scientific advice may overstep its basis in science. This leads us to recommend that **expert deliberation and public engagement exercises should report their conclusions not in the form of simple prescriptive findings but as properly qualified 'plural and conditional' advice** [paragraph 5.46].

10.9 Although we are critical of the emphasis placed on the contribution of biotechnology to national economic growth we also note that 'societal challenges' can be an equally limiting notion if used unreflectively as a focus for technological innovation. Economic growth is not itself a bad thing, although its blind pursuit may obscure other values. On the other hand, if growth were of paramount importance it is not clear that emerging biotechnologies are necessarily among the best ways of pursuing it. Yet merely replacing one precarious vision of the impact of biotechnology (economic prosperity) with another (that it will address urgent health or environmental problems, for example) can still obscure the real opportunity costs, whether these involve different technological approaches or other types of measure altogether. Without public reflection on this, at the very least policies cannot be known to be robust in the face of uncertainty. We therefore conclude that **when framing science policy through societal challenges, a 'public ethics' approach should be taken to avoid an overemphasis on technological rather than social solutions to problems with substantial social dimensions** [paragraph 6.37].

10.10 We note that competition for funding in recent years has increased the temptation for researchers to speculate about the impact of their research, and to speculate in very particular ways (for example, quantitative economic benefit). We conclude that **public systems for the allocation of research funding should be designed to avoid encouraging researchers to overstep the bounds of their competence when assessing the impacts of their research in non-research contexts** [paragraph 6.46]. Researchers themselves have a responsibility to resist pressure to engage in inflationary cycles of promises and expectations, since this may both mislead policy and result in distrust of science and technology, particularly where their statements inform public discourse on biotechnologies. We conclude that **those engaging in public discourse should not only accept responsibility for the factual accuracy and completeness of information they present but also use their best endeavours to ensure, through their continued participation in this discourse, that it is appropriately qualified and interpreted when represented by others** [paragraph 6.53]. We find, however, that the pressure within the policy process for definitive and unambiguous answers can, as with public engagement, also compromise the integrity of scientific advice to policy makers. When they participate in the public policy process, scientists involved in giving policy advice have a particular responsibility to exercise self-restraint and vigilance to avoid projecting a false sense of 'scientific certainty'.

10.11 Responding to the demands of funding and policy making bureaucracies inevitably means that the representation of research is framed by the rubrics of grant applications and prescribed kinds of social and economic impacts. We find that where there is not an engaged public discourse on science and technology it is possible to lose sight of the public good that

orientates research. We conclude that there should be more room for researchers to assert that their work has public good that goes beyond simple economic benefit. Likewise we conclude that the policy discourse on biotechnology can be limited by the way in which technical advice is obtained and technical 'experts' identified, including a tendency to fall back on established sources. Therefore we recommend that **in all cases in which technical advice is sought by policy makers there should be a demonstrable attempt to avoid sole reliance on a limited range of established experts in particular fields** [paragraph 6.58].

10.12 Turning to the formation of research and innovation policy we find that the discourse on policy frequently refers to a number of recurrent assumptions for which there is limited historical evidence. In particular, the dominance of economic values in the framing of research policy privileges arguments that can be made in terms of quantifiable economic impact over the significance of other values. In order to enable a balanced deliberation on normative values, one that can have an appropriate impact on policy, we conclude that **the determination of biotechnology policy should attend explicitly to diverse perspectives and bodies of evidence rather than privileging a single, quantitative frame of evaluation (such as economic costs and benefits, or costs and benefits reduced to economic values)**; this should be the case not only at the 'macro' level of Government policy but also at the 'meso' level of funding bodies and, indeed, at the 'micro' level of research [paragraph 7.32].

10.13 We find that the reasons states fund research are more complex than simply that knowledge is a 'public good' that would not be adequately provided by private firms, institutions or agents. The real reasons mix, for example, ideology, national self-image and strategic advantage, with the pursuit of economic growth, but they should be closely examined if policy is to be put on a more robust footing. That is not to say that the public good cannot be promoted by state funding of research and, given the dominance of private interests, such funding might be targeted at research supporting the creation of knowledge available to all that could counterbalance the sometimes aggressive promotion of products and techniques by vested interests.

10.14 Despite the uncertainties of emerging biotechnologies and the complexities and contingencies of innovation systems, research policy is ostensibly driven by notions of exploitability. Despite this we find that there is little assessment of the past success of this approach. We conclude, therefore, that **there is a need for serious evaluation and assessment of past research policies, both of Government as a whole and of particular public funding bodies, to understand in what conditions, if any, selective approaches to support for biotechnology are plausible** [paragraph 7.46].

10.15 Emerging biotechnologies are subject to significant uncertainties, partly as a consequence of the ignored complexity and contingency of the innovation system, partly due to the sensitivity of technology trajectories to contingent factors, and partly due to the possibility of encountering unanticipated 'hard' constraints. In the light of this we conclude that **policy makers should consider adopting an approach to social objectives that fosters diversity of research approaches, not just within the particular domains of individual funding bodies but across physical and life sciences, and the social sciences, combined with selective conditions of innovation that involve social benefit rather than just market value** [paragraph 7.48]. This approach offers a third way between 'picking winners' (whereby public authorities try to pick the most promising research for funding at an early stage) and leaving the selection of technologies to the market and economic determinants, by bringing additional factors, such as social value, into the set of evolutionary conditions that shape and filter technological trajectories.

10.16 Reviewing the sites of policy making and the actors involved, UK research policy appears to be shaped through an engagement between academic, political and industrial actors and framed by shared and persistent, but unexamined, cultural assumptions. Broader engagement does not come early enough in the process or at a high enough level to challenge these assumptions. In accordance with our approach to public ethics we recommend that **research policy should be framed not by received assumptions but through continuous engagement with a broad range of societal interests and with the involvement of social actors who can bring**

understanding of these interests to the joint enterprise of constructing a public frame for research policy decisions [paragraph 7.55].

10.17 We have noted throughout our enquiry, the privileging of economic framing of research policy to the neglect of other, important values and the need to rebalance these through a public discourse ethics. One barrier to this is the way in which research policy is concentrated in the Government department orientated towards business (the Department for Business, Innovation and Skills) and therefore much more accessible to business interests than others. This is one area in which we believe some structural reorganisation to be desirable, along the lines originally proposed by Lord Haldane, and therefore recommend that **consideration should be given to bringing Government research policy and funding bodies under a senior minister (i.e. of Cabinet rank) free from departmental responsibilities to ensure that research properly reflects all the objectives of Government, rather than those of a particular department** [paragraph 7.56].

10.18 As a bulwark against the framing of Government research policy by the preoccupations of a particular department or sector **there should be a clearly defined, written and published Governmental research policy against which detailed elements of departmental and other public research policies (such as the approach and methods of funding bodies) may be assessed**; this should not be produced, as it was formerly, by the Treasury [paragraph 7.56]. This should, as we have said, incorporate the promotion of diversity in underpinning research and the filtering of applied research and development according to a broad range of values rather than merely economic benefit.

10.19 Just as with public engagement, we find that the there is no *a priori* ideal system of regulation for emerging biotechnologies, and we recognise that regulatory design always involves dilemmas. Our conclusions are, in general, cautious: emerging biotechnologies may challenge the categories and modes of appraisal on which regulation depends and regulation may be either stifling (being adapted to incumbent technologies) or inapplicable to them. There is no single principle of regulatory design that can anticipate these problems: effective regulation of emerging biotechnologies must co-evolve alongside the technologies within a context created by public ethics.

10.20 The commercialisation of emerging biotechnologies depends substantially on protection of intellectual property via the patent system. We conclude, however, that this system fails substantially to optimise the social value from biotechnology innovation and that the field is better suited to public and collaborative systems, rather than market competition. Nevertheless the commercial sector has an important role to play in applied research, development and production of biotechnology products, and measures should be considered to align commercial interests with public good. Greater openness is conducive to this and **innovation should be included in corporate social responsibility reports as a separate, specific issue** [paragraph 9.53].

10.21 However, we conclude that more can be done, through intervention in the market, to overcome the failure of markets to maximise social benefit and to align commercial incentives with public good. This may be achieved by separating the rewards that innovators receive for the social value of their innovations from revenue they gain through the market price of the commercial product. Whereas the product, whatever it may be, would then be available at or around the economic cost of production, the value of the public good implied within it would be reflected in a separate payment. Therefore we recommend that **consideration should be given to state interventions in the market for new biotechnologies to secure the social benefits of innovation through direct reward for socially valued innovations** [paragraph 9.56]. In the Report we consider supplementary impact payment schemes as an example of such an approach, based on a comparative assignment of social value that is determined in accordance with the virtues and procedures of public discourse ethics.

Appendices

Appendix 1: Method of working

Background

The Nuffield Council on Bioethics established the Working Party on 'Emerging biotechnologies' in January 2011. The Working Party met eleven times over a period of 18 months. In order to inform its deliberations, it held an open consultation and a series of 'fact-finding' meetings with external stakeholders and invited experts. It also commissioned two reports on topics relevant to the work of the project and received comments on a draft of the Report from 12 external reviewers. Further details of each of these aspects of the Working Party's work are given below and in Appendix 2. The Working Party would like to express its gratitude to all those involved for the invaluable contribution they made to the development of the final Report.

Consultation document

The Working Party launched a consultation in April 2011, which ran until July 2011. 84 responses were received, of which 48 were submitted by individuals and 36 on behalf of organisations. Those responding to the consultation included students, academics, faith groups and professional organisations. A full list of those responding is set out in Appendix 2. A summary of the responses is available on the Council's website. Copies of individual responses will also be made available on the website in those instances where the Council has permission from respondents to do so.

Fact-finding

As part of its work, the Working Party held a series of 'fact-finding' meetings, the details of which can be found below. (Details reflect affiliations at the time of the meetings.)

Research and development: 6 May 2011

- **Dr Jim Ajioka**, Department of Pathology, Parasitology Group, University of Cambridge
- **Professor Robert Brown**, Head of Tissue Repair and Engineering Centre, University College London
- **Professor Keith Campbell**, Professor of Animal Science, Nottingham University
- **Professor Olivier Danos**, Cancer Institute, Gene Therapy Group, University College London
- **Mr Alexander L Green**, Spalding Senior Lecturer and Consultant Neurosurgeon, John Radcliffe Hospital, Oxford
- **Professor Richard Kitney OBE**, Professor of Biomedical Systems Engineering, Imperial College London
- **Professor Dek Woolfson**, School of Biochemistry, University of Bristol

The role of public engagement: 6 May 2011

- **Professor Martin Bauer**, Head of the Methodology Institute and Professor of Social Psychology and Research Methodology, London School of Economics and Political Science
- **Mr Simon Burall**, Director, Involve
- **Dr Jason Chilvers**, Lecturer in Environmental Management, University of East Anglia
- **Dr Clare Matterson**, Director, Medical Humanities and Engagement, Wellcome Trust
- **Dr Patrick Middleton**, Head of Public Engagement, BBSRC
- **Dr Alison Park**, Head of Society and Social Change, National Centre for Social Research
- **Dr Tom Wells**, Department for Business, Innovation and Skills

Intellectual property, innovation and markets: 24 June 2011

- **Dr Graham Bell**, TSB
- **Dr Nicki Curtis**, Senior Policy Advisor, IPO
- **Dr Tim Harper**, Director, Cientifica
- **Professor Douglas Kell**, Chief Executive, BBSRC

- **Dr Denis Koltsov**, Information Manager, the Nanotechnology Industries Association
- **Dr Steve Musgrave**, Founding Partner, Unicorn Biologics
- **Ms Vicki Salmon**, Partner, IP Asset
- **Dr Nigel Sansom**, Senior Manager for Technology Introduction, NHS Innovation
- **Dr Richard Seabrook**, Business Development Manager, Wellcome Trust

Policy, regulation and governance: 8 July 2011

- **Dr Mark Bale**, Interim Director, Health Science & Bioethics Division, Department of Health
- **Dr Tim Brooks**, National Specialist, Centre for Emergency Preparedness and Response, Rare and Imorted Pathogens Laboratory, HPA
- **Professor Jim Dunwell**, Member of ACRE
- **Dr Neil Ebenezer**, Head of New and Emerging Technologies, Devices Division, MHRA
- **Dr Katherine MacGregor**, Policy Advisor, Royal Academy of Engineering
- **Professor Robin Lovell-Badge**, Academy of Medical Sciences
- **Dr Catherine Rhodes**, Institute for Science, Ethics and Innovation, University of Manchester
- **Dr Jack Stilgoe**, Senior Research Fellow, University of Exeter
- **Ms Hilary Sutcliffe**, Director, MATTER
- **Professsor David Wield**, Director, ESRC Innogen

Evidence reviews

In order to inform its deliberations, the Working Party commissioned two additional reports. These covered: the sources and allocation of funding for research and development of biotechnologies; and, the analytical significance of the concept and property of 'emergence' in the patent system.

The terms of each review are set out below.

Review 1: Emerging biotechnologies: can we find out who funds R&D and what they support?

Purpose: to assist the Working Party in understanding:

1. existing patterns of national and international research funding (or resource allocation) in the field of biotechnology; and

2. the extent to which these data can be reasonably acquired and the limitations of the relevant methodologies.

The review was carried out by Dr Michael Hopkins of SPRU (Science and Technology Policy Research), University of Sussex. The review did not seek to provide a comprehensive analysis of existing sources providing data on biomedical funding but, rather, presented illustrations of the forms in which data are available.

Review 2: The analytical significance of emergence in the patent system

Purpose:

1. to assist the Working Party in understanding the intellectual property system as it applies to emerging biotechnologies and, in particular:

    - challenges for the IP system posed by emerging biotechnologies and how the IP system has responded/might respond to these; and

    - challenges posed by the IP system for emerging biotechnologies and how the practitioners have responded/might respond to these

2. To provide data and concrete examples to support this analysis

3. To assist the Working Party to draw conclusions about how decisions about IP conditions that influence (limit, facilitate, control, direct, etc.) the emergence of biotechnologies should be framed and advice that should be taken into consideration.

The review was carried out by Dr Siva Thambisetty, London School of Economics and Political Science and was informed by work on an EPSRC Discipline Hopping Award on synthetic biology. The review was largely based on secondary research.

External review

An earlier version of this Report was reviewed by 12 individuals with expertise in disciplines relevant to different aspects the project. These individuals were:

- Dr Tavis Bayer
- Professor Julia Black
- Professor Martin Bobrow
- Professor John Dupré
- Dr Yasemin J Erden
- Dr Shawn Harmon
- Professor Stephen Hughes
- Professor Sheila Jasanoff
- Dr Paul Nightingale
- Professor Judith Petts
- Professor Dietram A Scheufele
- Professor Philip Scranton

The Working Party deeply appreciates the time and thought the reviewers brought to this task and thanks them for their helpful contributions.

The views expressed within this Report are those of the Working Party and the Council and do not necessarily reflect the views of any participants in the various activities undertaken by the Working Party in connection with this Report.

Appendix 2: Wider consultation for the Report

The aim of the consultation was to obtain views from as wide a range of organisations and individuals interested in the area as possible. The consultation document was published online and made available in hard copy on request. Individuals and organisations that the Working Party expected to have a particular interest were also directly alerted by email and encouraged to respond. The document was divided into three main substantive parts:

- the nature and identity of emerging technologies;
- the cultural, international and historical context; and
- the relevant ethical, policy and public engagement issues.

In total, 17 questions were posed, and respondents were encouraged to answer as many, or as few, as they wished. Eighty four responses were received, 48 from individuals and 36 from organisations. Eight respondents wished to remain anonymous. All the responses were circulated to Working Party members and a summary of responses was considered in detail at a subsequent Working Party meeting.

A summary of the responses received, together with the original consultation paper, is available on the Council's website.[706] Individual responses will also be published in full on the website, where respondents have given permission for the Council to do so. The responses received played an important role in shaping the Working Party's thinking, and the Working Party is grateful to all those who contributed.

Anonymous

Eight respondents wished to remain unlisted.

Individuals

- Professor Jayapaul Azariah, Founder President, All India Bioethics Association
- S. Bonny
- Professor Derek Burke
- Professor Raphael Cohen-Almagor, University of Hull
- Mr K.R Coleman
- Dr Otakar Fojt, Science and Innovation Network, British Embassy Prague
- Dr Sara Fovargue, Law School, Lancaster University
- Dr Caroline E Foster
- Dr Christopher French
- Professor Robert T Hall, Profesor de Bioética, Facultad de Química, Universidad Autónoma de Querétaro, Mexico
- Dr Olivia Harvey
- Jonathan Harwood
- Elisabeth Hildt, University of Mainz
- Yutaka Hishiyama

[706] See: http://www.nuffieldbioethics.org/emerging-biotechnologies/emerging-biotechnologies-consultation.

- David S Jones, Massachusetts Institute of Technology
- Masaru Katoh
- Drew L Kershen, Professor of Law (USA)
- Leicester Medical School – Jake Smith, Ruth Jones, Ashish Patel, Aaron Dean, Catherine Heighton, Safiyah Surtee, Charu Thanvi, Callum Johnson, Joe Mortimer
- Leicester Medical School – Josh Brewin, Philip Cheng, Atyeh Hamedani, Odin Leung, Manisha Munyal, Francis Okoroh, Preeya Ummur, Anna Weatherill and Abigail Western.
- Leicester Medical School – Group 21
- Leicester Medical School – Louise Newton, Suzanne Holmes, Nicholas Green, Sasha Denny-Morley, Kassir Mahmood, Jognesh Mistry, Imran Ahmed
- Leicester Medical School – Rebecca Pierce, Rosie Allen, Edward Rogers, Krupa Samani, Amy Forsyth, Heather Buckby, Rae Clark, Abdul Hassan
- Leicester Medical School – David Ademidun, Wayne Mitchell, Jennifer Kwan, Chloe Thomson, Jonaid Farid, Cara Booth, Francesca Lorford, Susannah Gurung, and Andrew Mabey
- Stefania Lymperi, PhD and Takis Vidalis, PhD, Senior Scientist, Hellenic National Bioethics Commission
- Luc Michel, Surgical Services, Catholic University of Louvain at Mont-Godinne Hospital
- Professor Vivian Moses
- Thomas E Nickson, PhD, Monsanto Company, St Louis, MO USA
- Inès Violeta Ortega Garcia
- Simone Penasa
- Professor Maude Phipps, Jeffrey Cheah School of Medicine & Health Sciences, Monash University
- Powell, Buchanan, Douglas & Savulescu
- Megan Quinlan, representing the MosqGuide Project, Imperial College London
- Mertxe de Renobales Scheifler, University of the Basque Country/EHU, Spain
- Sal Restivo & Sabrina Weiss, Renssalaer Polytechnic Institute
- Professor Bonnie Steinbock
- Hilary Sutcliffe - MATTER
- Professor Kevin Warwick
- Professor Sir David Weatherall
- Dr Alan R Williamson
- Go Yoshizawa, University of Tokyo

Organisations

- Agricultural Biotechnology Council (ABC)
- Bio Ethics Group, The Church in Wales
- British Embassy, Washington DC
- British High Commission Singapore
- British Medical Association
- British Science Association
- Centre for Bioethics & Emerging Technologies, St Mary's University College London
- Cesagen (ESRC Centre for Economic and Social Aspects of Genomics)
- Christian Medical Fellowship
- Egenis, University of Exeter
- ESRC Innogen Centre
- Federal Ethics Committee on Non-Human Biotechnology
- GeneWatch UK

- Government Office of Science, Department for Business, Innovation & Skills, Science and Innovation Network - Finland
- HEAL UoS (Health, Ethics and Law, University of Southampton) and CELS (Clinical Ethics and Law at Southampton)
- HeLEX Centre for Health, Law and Emerging Technologies; University of Oxford
- Humanist Society of Scotland
- John Innes Centre
- Medical Ethics Alliance
- Nishat Hyder, on behalf of ISEI and CSEP, University of Manchester
- Nowgen
- PHG Foundation
- Professor Nick Pidgeon, Cardiff University
- RCOphth (NB submission from Prof Dua, president of RCOphth)
- Research Councils UK
- Reverend Dr McCarthy, National Adviser, Medical Ethics and Health and Social Care Policy, The Archbishop's Council, the Church of England
- The Royal Academy of Engineering
- RSPCA
- Science and Innovation Network - India
- Science, Culture and the Law (SCuLE), University of Exeter School of Law
- Sense about Science
- UK Science and Innovation Network - Canada
- UK Science and Innovation Network - Switzerland (response compiled by Gaby Bloem)
- Antonio G. Spagnolo, Institute of Bioethics, School of Medicine "A. Gemelli", Università Cattolica del Sacro Cuore - Roma
- Value Addition to Genomic and GE3LS (VALGEN)
- Wellcome Trust

Appendix 3: The Working Party

Professor Michael Moran (Chair)

Michael Moran is Professor Emeritus of Government at the University of Manchester. His main interests lie in regulation, especially economic regulation. His publications include *Governing the Health Care State* (1999), *The British regulatory state* (2007) and *After the Great Complacence: financial crisis and the politics of reform* (2011).

Dr Jane Calvert

Jane Calvert is Reader in Science, Technology and Innovation Studies at the ESRC Innogen Centre. Her broad area of research is the sociology of the life sciences. She is currently studying the emergence and development of systems biology and synthetic biology. She is particularly interested in the role of social scientists in new scientific fields, the differences between biology and engineering, intellectual property and open source, and design and aesthetics in synthetic biology.

Mr Trevor Cook

Trevor Cook is a partner in the international law firm Bird & Bird LLP. He specialises in patent and other intellectual property litigation and advice and life sciences administrative law. In addition to numerous articles and several co-authored publications, he has written the following books – *A User's Guide to Patents* (2011), *EU intellectual property law* (2010), *Pharmaceuticals, biotechnology and the law* (2009), *A European perspective as to the extent to which experimental use, and certain other, defences to patent infringement, apply to differing types of research* (2006) and *The protection of regulatory data in the pharmaceutical and other sectors* (2000).

Professor David Edgerton

David Edgerton is Hans Rausing Professor at Imperial College London. He is the Founding Director of its Centre for the History of Science, Technology and Medicine. His most recent books are *The shock of the old: technology and global history since 1900* (Profile 2007) and *Britain's war machine: weapons resources and experts in the Second World War* (Allen Lane/Penguin, 2011).

Professor Ray Hill

Ray Hill was Head of Licensing and External Research for Europe at Merck, Sharp and Dohme until his retirement in May 2008. He is a pharmacologist with a special interest in pain and headache research and is a Visiting Professor at Imperial College London and Bristol, Surrey and Strathclyde Universities. He is a non-executive Director of several biotech companies and Honorary Biomedical Business Development Advisor at Imperial College London. He is President Emeritus of the British Pharmacological Society.

Professor Søren Holm

Søren Holm is Professor of Bioethics at the University of Manchester and part-time Professor of Medical Ethics at the University of Oslo, Norway. He is a medical doctor and philosopher and a former member of the Danish Council of Ethics. He is the former President of the European Society for Philosophy of Medicine and Health Care and former Editor in Chief of the *Journal of Medical Ethics*. He currently edits the journal *Clinical Ethics*.

Professor Richard A.L. Jones

Richard Jones is Pro-Vice-Chancellor for Research and Innovation at the University of Sheffield, is an experimental physicist whose own research concentrates on the properties of macromolecules at surfaces and interfaces. In his work in nanotechnology he is interested in learning from the principles used by cell biology to create synthetic, functional nanodevices. Professor Jones has also developed

a more general interest in nanotechnology and its potential impact on society, and has been extensively involved in public engagement around nanotechnology.

Professor Eli Keshavarz-Moore

Eli Keshavarz-Moore is Professor of Bioprocess Science and Enterprise at University College London. Her research interest is in the bioprocessing of complex macromolecules with therapeutic promise including fusion proteins, antibody fragments (monoclonal and polyclonal), artificial chromosomes and phages; and cells including microbial, mammalian and fungal systems as well as transgenic materials. She is one of the Principal Investigators in the Innovative Manufacturing Research Centre in Bioprocessing. Since 2000, Professor Keshavarz-Moore has led the development and implementation of innovative enterprise training and commercialisation of research opportunities at the bioprocessing/life sciences interface including a leadership programme for Senior Executives in the Bioscience industries.

Professor Noel Sharkey

Noel Sharkey is Professor of Artificial Intelligence and Robotics and Professor of Public Engagement at the University of Sheffield (Department of Computer Science). He has moved freely across academic disciplines, lecturing in engineering, philosophy, psychology, cognitive science, linguistics, artificial intelligence, computer science and robotics as well as lecturing extensively to the public, policy makers and the military. Noel's core research interest is now in the ethical application of robotics and AI in areas such as military, child care, elder care, policing, telepresence, transport and medicine. He is currently a Leverhulme Research Fellow for an ethical and technical appraisal of Robots on the Battlefield.

Professor Andrew Stirling

Andy Stirling is Professor of Science and Technology Policy and Research Director at SPRU (Science and Technology Policy Research) at the University of Sussex. He has a background in natural and social science, working formerly as an archaeologist, then a disarmament and environment activist. For 20 years, he has been an interdisciplinary researcher and policy adviser, focusing on challenges in the governance of science, technology and innovation. He has published widely on these issues and served on several public advisory bodies in the UK and EU.

Professor Patrick Sturgis

Patrick Sturgis is Professor of Research Methodology at the University of Southampton and Director of the ESRC National Centre for Research Methods. He is Principal Investigator of the Wellcome Trust Monitor study and President of the European Survey Research Association. His main research interests are in the areas of survey and statistical methods, public opinion and political behaviour, particularly regarding social cohesion and trust and public attitudes to science and technology.

Professor Andrew Tylecote

Andrew Tylecote is Emeritus Professor of the Economics and Management of Technological Change at the University of Sheffield. His background extends across the social sciences, and his research has ranged widely around the broad question: how do social and economic institutions affect technological change and economic development? He has been Treasurer of the European Association for Evolutionary Political Economy, and Visiting Professor at Tsinghua and Zhejiang universities, China. He was joint winner of the Myrdal Prize for his book with Francesca Visintin on *Corporate governance, finance, and the technological advantage of nations* (Routledge, 2007).

Glossary

Emboldened, italicised entries are terms used in this report with a specific meaning. Other italicised words refer to entries found elsewhere in the glossary, except where they denote titles.

***Ambiguity*:** lack of agreement about the implications, meanings or relative importance of a given range of possible outcomes (irrespective of the likelihood of their occurrence). Ambiguity reveals the association of different and possibly incompatible meanings and values with the practices, products and consequences of biotechnologies.

Angel investor: a wealthy individual who invests in new businesses in return for pre-agreed financial return. Angel investors differ from venture capitalists in that the capital invested is usually owned by the investor. They sometimes operate collectively.

Antisense: a field of research within biomedical science focusing on preventing the progression of disease by making inactive the genes responsible. It involves introducing a strand of ribonucleic acid with a molecular composition that binds to genes identified as responsible for replication of disease in order to suppress their expression.

Asbestos: naturally occurring, fine mineral fibres which are highly heat-resistant and used in brake linings thermal insulation, fire resistant fabrics, (asbestos) cement, etc. Due to the major health hazards of the loose fibres and dust, its usage is now prohibited for some applications.

Avian flu: a naturally occurring genus of the influenza virus that is maintained in wild birds but also affects commercial and pet birds and can (rarely) infect mammals. There are multiple sub-types of the influenza A virus which can be divided into viruses of high and low levels of harmfulness. It is difficult for avian influenza viruses to infect humans but in 1997 the highly-pathogenic influenza A virus sub-type H5N1 emerged in Hong Kong and transmitted to humans, in some cases fatally.

Bioart: the creation of artworks from biological material including genetically modified organisms and artefacts.

Biodiversity: the genetic, taxonomic and ecosystem variety in the living organisms of a given area, environment, ecosystem or planet.

Bioeconomy: economic activity that is fuelled by research and innovation in the biological sciences.

Bioethics: a branch of *ethics*. Since the 1970s the term has been used to refer to the study of ethical issues arising from the biological and medical sciences.

Bioinformatics: a scientific discipline concerned with biological data, specifically the storage, transmission, retrieval and analysis of such data.

Bioreactor: an artificial device for the purpose of processing cells (or cell components) into desired products. This includes organisms modified to produce particular substances that they would not otherwise be able to produce. See *pharming*.

Bioremediation: the use of living organisms to absorb pollutants (usually in soil or water) in order to decontaminate a particular environment.

Biosafety: the safe handling and containment of infectious microorganisms and hazardous biological materials, applicable to humans, animals and the environment.

Biosecurity: securing biological materials in the context of military and national security risks. More generally, biosecurity can be understood as the protection of living organisms from harmful effects brought about by other species, especially the transmission of disease, although there is no single accepted definition of the term.

***Biotechnology wager*:** the idea that in order for more people to enjoy longer, healthier, richer and more comfortable lives, it is as if society has – collectively – made a wager on the technologies of the future supplying the means continuously to outrun the costs of consumption and growth.

Bricolage: a word of French origin meaning the assembly of an artefact or the solution to a practical problem using whatever resources are at hand. The term has slightly different meanings across disciplines. In philosophy, the term is associated in particular with the work of Claude Lévi-Strauss, to describe a form of thought that arrives at solutions using multiple, sometimes unrelated, methods and concepts. In biology, it occurs in the metaphor of evolutionary processes as "a tinkerer, engaged in piecemeal construction."[707]

Chimera: an animal comprised of whole cells from two or more different organisms.

Chlorofluorocarbons (CFCs): compounds consisting of ethane or methane with some or all of the hydrogen replaced by fluorine and chlorine. Used as refrigerants but their usage is now depreciated because they destroy atmospheric ozone and thus contribute to the greenhouse effect.

Citation impact: academic citations (references) used as a measure of usage and impact. Can apply to individuals, organisations or pieces of work. (See also *field weighted citation impact.*)

Clinical trial: a way of testing the efficacy of a treatment or a hypothesis related to the cause of a disease. 'Phase 1' trials evaluate safety and dose of a prospective treatment. 'Phase 2' trials evaluate effectiveness. 'Phase 3' trials confirm effectiveness and safety in preparation for wide-scale use.

Collingridge dilemma: a problem associated with the English social philosopher David Collingridge who suggested that attempting to control a technology is difficult because during its early stages, when it can be controlled, not enough can be known about its harmful social consequences to warrant controlling its development; but by the time these consequences are apparent, control has become costly and slow.

Consumer surplus: the excess of the benefit a consumer gains from the purchase of a good over the amount paid for the good. Can be measured by the by the area below the demand curve but above the price. (See also *producer surplus.*)

Defense Advanced Research Projects Agency (DARPA): an agency of the US Department of Defence tasked with maintaining the technological superiority of the US military and preventing 'technological surprise' from harming the national security of the US.

DIY biology/'Do it yourself' biology): 'amateur' individuals or groups undertaking or initiating biological experiments, processes or activities with little or no professional or institutional affiliation or oversight. Often performed as a hobby.

DNA: deoxyribonucleic acid; the chemical that carries a person's genetic information. Most cells of a person's body contain a complete copy of that information. A DNA molecule consists of a long chain of units called nucleotides or 'bases'. There are four sorts of nucleotides: guanine, adenine, thymine, and cytosine.

Dual-use: a term applied to the tangible and intangible features of a technology that enable it to be applied to both hostile and peaceful ends with no, or only minor, modifications.

Ethics: a branch of philosophy concerned with the study of values and moral reasoning, and their application to human conduct.

[707] Wilkins AS (2007) Between "design" and "bricolage": genetic networks, levels of selection, and adaptive evolution *Proceedings of the National Academy of Science* **104**: 8590-6.

Field-weighted citation impact: an indicator of quality that adjusts for differing citation practices in different subject fields and therefore of the different subject emphases of comparator countries. (See also *citation impact.*)

Frame: broadly, a background of knowledge, beliefs and values that give a particular significance to different possible objects of contemplation. The concept of a 'frame' has different meanings across various disciplines including sociology, communication studies and cognitive psychology. In particular, the concept is associated with the sociologist Erving Goffman and his book *Frame analysis* in which he defined a frame as "definitions of a situation…built up in accordance with principles of organization which govern events – at least social ones – and out subjective involvement with them".

Framework programme(s): the 'Framework Programmes for Research and Technological Development' are multi-year EU funding programmes. As of 2012, there have been seven such programmes. Framework seven is due to end in 2013. Research priorities vary between programmes.

Free rider: those who partake of the benefits of some cooperative enterprise without contributing to it.

Full-cost accounting: an accounting technique that recognises multiple types of 'value', including financial, social and environmental.

Gene therapy: treating disease caused by faulty genes or gene function by the introduction of new therapeutic genes directly into the patient's cells by means of vectors, such as modified viruses.

Gene: the fundamental unit of inheritance. A gene is an ordered sequence of nucleotides located in a particular position on a certain chromosome that encodes a specific functional product (i.e. a protein or RNA molecule).

Genetic modification: the direct introduction of specific characteristics by artificial transfer of functional genes into an organism.

Genome: the full complement of genetic material in the cells of an individual organism or species; the totality of the DNA sequences of an organism or organelle.

Green revolution: a range of practices and technologies (including chemical pesticides, fertilisers, irrigation and plant breeding) that transformed agricultural food production in the decades following the 1940s, in particular through technology transfer to developing countries.

Gross domestic product (GDP): the total market value of all goods and services produced within a country in a specific period of time.

Gross national product (GNP): the total market value of all goods and services produced by the residents of a country in a specific period of time, including value produced by nationals working abroad and excluding value produced by foreign nationals working in the relevant host country.

H5N1: see *avian flu*.

Haber-Bosch process: a process of fixing nitrogen, in which the nitrogen is made to combine with hydrogen under influence of high temperature, high pressure and a catalyst for the purposes of creating ammonia, which is then usually used in the production of fertiliser.

Health impact fund: a method proposed as a way of remedying the perceived failure of the global pharmaceutical development and distribution system to attend properly to the needs of certain subpopulations. It is designed to reward pharmaceutical firms that develop drugs mainly for use in developing countries.

Higher Education Funding Council for England (HEFCE): a non-departmental public body of the Department for Business, Innovation and Skills in England, responsible for distributing public money for higher education to universities and colleges in England, for the purposes of research, education and related activities; HEFCE's focus is on funding research infrastructure. Compare to the *research councils*, which provide funding for specific research projects and programmes.

Human Genome Project: a 13-year international project established in 1990 to coordinate the sequencing of the 2.85 billion nucleotides that make up human DNA. The first draft was published in 2001.

iGEM Foundation: 'International Genetically Engineered Machine Foundation'; an organisation dedicated to education and competition, advancement of synthetic biology, and the development of open community and collaboration.

In silico: a term used to describe bioscientific experiments carried out using a computer (i.e. on a silicon chip).

In vitro fertilisation: fertilisation 'in glass' (i.e. in the laboratory), as opposed to in the body (*in vivo*). Eggs are removed from the body (often following artificial stimulation of the ovaries) and mixed with or injected with sperm. A resulting embryo may then be transferred to a woman's uterus with the intention of establishing a pregnancy.

Innovation and Knowledge Centres: specialised centres of UK scientific excellence, granted five years' funding from a UK research council or the Technology Strategy Board in order to accelerate and promote business exploitation of an emerging research and technology field.

Intellectual property: an intangible form of personal property. Patents, copyrights, trademarks, service marks, trade names and trade secrets are examples of intellectual property.

Knowledge economy: an economy the focus of which is information rather than physical products or processes (mining or manufacturing, for example). This may be a focus on the production of information or a focus on physical production or processes based on particular types of information.

Lock-in: the idea that specific technological pathways, although not inevitable in advance, once embarked upon become progressively difficult and costly to escape.

Monoclonal antibody: antibody produced by a single clone of cells or a cell line derived from a single cell. Such antibodies are all identical and have unique amino acid sequences.

Nanomedicine: the use of nanotechnological techniques or materials for medicinal purposes.

Nanotechnology: the basic and applied science concerning materials at a scale of up to 100 nanometres. A nanometre is one billionth of a metre (1×10^{-9} metres).

National Health Service: the name applied to the publicly-funded healthcare services that operate in the constituent countries of the UK.

Open source: an approach to design, development, production and distribution that seeks to encourage and enable public access to the fundamental resources upon which a product is based or constructed. Commonly applied to software engineering where the source code would be published freely, the term it is now applied to many fields including, for example, synthetic biology.

Opportunity cost: the cost of something in terms of an opportunity foregone when it is chosen, i.e. the benefits that could have been obtained by choosing the best alternative opportunity. Sometimes used loosely to describe situations where the characteristic of *ambiguity* can mean that opportunities foregone may actually be more highly valued by some subpopulations within society, despite being more highly valued by others who may have the power to select them.

Optical tweezers: a beam of light that exerts force in the piconewton range that is sufficient to move small organelles around under a microscope or to measure the forces that motor molecules are exerting.

Orphan drug: a pharmaceutical developed and produced for a patient population that too small to be considered economically feasible to provide for under standard pharmaceutical industry business models.

Patent: the right, granted by a government, to exclude others from making, using or selling an invention.

Path dependency: a concept that describes how prior contingent choices constrain subsequent ranges of options. It was primarily developed within the field of economics to explain why certain technological 'paths' have been taken in preference to others. It is also used in a number of other disciplines, such as the political and social sciences, being adapted to the relevant context.

Personalised medicine: a concept that reflects a confluence of different scientific, technological and social disciplines and approaches. It has a number of different meanings, but among these is the tailoring of medicine to the biological characteristics of particular patients or patient groups (pharmacogenetics, stratified medicine). The basic enabling technology for personalised medicine is molecular diagnostics.

Pharming: the use of genetically modified animals as *bioreactors* to produce substances beneficial to humans, such as insulin for the treatment of diabetes and vaccines, which may be extracted, for example, from the animals' milk.

Phase 1/2/3 clinical trial: see *Clinical trial*.

Pluripotent: the capacity for some cells to differentiate into many, but not all, final differentiated cell types of an organism. Compare to multi- and toti- potent cells (respectively, the potential to give rise to a variety of limited cell types (the result based on environmental cues) and the ability to divide into all differentiated cell types of the relevant organism).

Polyketides: a class of drugs with a variety of uses, such as the production of antibiotics and insecticides.

Precautionary principle/approach: an approach often implemented in the field of technology regulation that arises from realisations about the limits of narrow, risk-based approaches when operating under conditions of uncertainty and ambiguity. Originally articulated in Principle 15 of the 1992 Rio Declaration on Environment and Development as: "In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." It is subject to disputed interpretation.

Pre-implantation genetic testing/diagnosis: a technique in which genetic testing of an *in vitro* fertilised embryo is carried out before the decision to implant the embryo is taken.

Producer surplus: the value of total sales revenue going to producers over the area above the supply curve and below the price for a good; the benefit that producers accrue by selling a product for an amount more than the lowest cost at which they would be prepared to sell that product. (See also *consumer surplus.*)

Public engagement: engagement between those accountable for a given range of practical decisions and those who have a 'public' interest in their outcomes.

***Public ethics*:** a concept of ethics used in this report broadly reflecting both a general reorientation away from an individualistic ethical tradition and recognition of an inherent public interest in biotechnologies. 'Public ethics' focuses on moral action that has broad social implications and is concerned with the formation of the context within which public decisions are made and by which they are framed (rather than the inclusion of a consideration of ethical implications as an element of the process of policy development and governance.)

Public good: a good that is non-rivalrous or non-excludable, or both. A good is non-rivalrous if my use of it does not in any way reduce the amount of it available for you to use. A good is non-excludable if it cannot be made available to you without also making it available to me and any number of others who might also wish to enjoy it.

Public sphere: a term which can be (broadly) understood to describe the social, intellectual and spatial phenomena of private actors joining in open, public discussion of societal issues. Primarily based on the work of Jürgen Habermas, in particular the book *The structural transformation of the public sphere*.

Quality-adjusted life year (QUALY): a method used to compare different pharmaceuticals and measure their clinical effectiveness. The UK National Institute for Health and Clinical Excellence (NICE) website notes that it is intended to "[give] an idea of how many extra months or years of life of a reasonable quality a person might gain as a result of treatment". NICE use the output of a QUALY measurement as a way of calculating cost-benefit.

Regenerative medicine: interventions that aim to provide for the repair of organs, tissue or cells. Often uses stem cells to replace damaged or diseased tissues.

Research and development (R&D): work directed towards the innovation, introduction and improvement of products and processes. The term is used primarily in the private sector.

Research council(s): the UK's research councils are publicly funded agencies responsible for investing public money in research in the UK. They provide funds for specific research projects and programmes. Compare to the *Higher Education Council for England*, which provides funds focused more on research infrastructure.

Research Excellence Framework (REF): a system for assessing the quality of research in UK higher education institutions.

Research intensity: a nation's gross expenditure on R&D measured as a share of that nation's *gross domestic product*.

Responsible innovation: governance of science and innovation that includes considerations of risk and regulation and the incorporation a collective approach to defining how science and innovation should influence the future; it considers questions of anticipation, reflexivity, inclusion and responsiveness.

Ribosome: a cell organelle made of ribosomal RNA and protein. It is the main site of biological protein synthesis.

RNA: ribonucleic acid, a molecule similar in structure to *DNA*. It is the main agent for transferring information from DNA to the protein-synthesizing machinery of cells, but can also hold genetic information (as it does in the case of viruses).

RNAi: ribonucleic acid interference; the blocking of gene expression by disrupting the translation of messenger *RNA* into proteins. When performed through artificial means it is often used to study gene function. The blocking of gene function also has theraputic potential.

Semiconductor: an element or compound having higher resistivity than a conductor but lower resistivity than an insulator. Semiconductor materials are the basis of diodes, transistors, thyristors, photodiodes and all integrated circuits ('silicon chips').

Sequencing: procedure for determining the sequence of nucleic acid or protein.

Sociotechnical imaginary: the way science and technology influence collective visions of good and attainable futures.

Spin-out/spin-off: either a subsidiary of a 'parent' organisation or an entirely new, independent organisation that has split-off from its parent. Commonly occurs in the context of a small, independent spin-out company formed by splitting off from a larger, parent, academic organisation (such as a university) for the purpose of profitable commercialisation of a technology developed originally within an academic setting.

Stem cells: non-specialised cells, which can divide indefinitely to produce either more stem cells or cells that commit to becoming more specialised (differentiated) cell types. Can be used in regenerative medicine to repair damaged or diseased tissues or organs.

Sustainability: as elucidated by the Brundtland Commission, "meeting the needs of the present without compromising the ability of future generations to meet their own needs."

Synthetic biology: the use of principles derived from biology, chemistry and engineering for the construction of novel biological networks/organisms with bespoke properties (or the re-construction of pre-existing organisms for specific purposes), using standardised biological parts that are well-characterised and have known functions.

System effects: the interdependency of elements within systems acting as an exponent of small, local effects, potentially leading to large-scale changes.

Technological determinism: the potential of a technology to determine the horizon of possibilities for society in a non-trivial way. That is, that the technologies in use exert a dominant or shaping force on society and social organisation.

Technological paradigm: a concept developed in technology studies literature to support evolutionary explanations of both continuous and discontinuous technical change.

Technological singularity/'the singularity': a notion expressing the overtaking of human intelligence by intelligence not of solely biological origin.

Technological trajectory: a concept closely related to that of the '*technological paradigm*'. Technological trajectories have been described as being the direction of technical advance within a certain technological paradigm; the 'pattern' of the normal technological progression inherent in the concept of technological paradigms.

Technology 'roadmapping': a process during which an attempt is made to identify, plan and record the requirements for goal-orientated technology development. May be used to articulate and promote collective visions for technology development.

Technoscientific imaginary: a label for the ways in which attitudes to prospective technologies are construed in terms of the kind of world that technological developments may bring about. These commonly incorporate features such as longevity, health into old age, free electricity/power, inexpensive consumption, etc., and corresponding dystopias, such as decimation by mutant pandemic viruses or the emergence of a 'genetic underclass'.

The Enlightenment: a Western intellectual movement of the late 17th and 18th Centuries emphasising reason and individualism rather than tradition.

Tissue engineering: a technique for addressing tissue and organ failure by implanting natural, synthetic, or semisynthetic tissue and organ mimics that are fully functional from the start, or that grow into the required functionality.[708]

***Transformative potential*:** the capacity that some emerging biotechnologies may have to transform or displace existing social relations, practices and modes of production, or create new capabilities and

[708] See: Nature Biotechnology editorial (2000) Tissue engineering *Nature Biotechnology* **18**, IT56-IT58.

opportunities that did not previously exist (or may not even have been imagined). These outcomes might be entirely unexpected or unsought.

Transhumanism: an ideology that valorises the transformation of the human condition through technologies, for example, to promote life extension or cognitive and physical enhancement.

***Uncertainty*:** an inescapable lack of knowledge about the range of possible outcomes or about the likelihood that any particular outcome will in fact occur. This seriously limits the possibility of accurately forecasting the consequences of decisions with regard to biotechnologies (positive or negative) and similarly limits the effectiveness of prospective efforts to control these outcomes.

Venture capital: capital whose owners are willing to invest in new or small businesses, where the risk of losing is high, usually in exchange for correspondingly high returns.

Xenobiology: a field of study which attempts to make a biology that is altogether different from that which is found in nature, such as attempting to use different kinds of nucleic acid, for example 'xeno-nucleic acid' (XNA) as opposed to the familiar *RNA* or *DNA*.

Xenotransplantation: the transplantation of organs, tissue or cells from one species to another.

The definitions above are derived from a number of sources. Significant, uncited, sources include several previous Nuffield Council reports; *Chambers dictionary of science and technology* (2007); *Oxford dictionary of philosophy*, 2nd edition (2008); *Taber's cyclopedic medical dictionary*, 21st edition (2009); O*xford dictionary of sociology*, 3rd edition (2009); *Concise Oxford English dictionary*, 12th edition (2011); and, *Oxford dictionary of economics*, 4th edition (2012).

List of abbreviations

AEBC	Agriculture and Environment Biotechnology Commission
BBSRC	Biotechnology and Biological Sciences Research Council
BIS	(Department of) Business, Innovation and Skills
BIVDA	British In Vitro Diagnostics Association
BPAA	Best previously available alternative(s)
BPF	Big pharmaceutical firm
DBF	Dedicated biotechnology firm
Defra	Department for Environment, Food and Rural Affairs
DNA	Deoxyribonucleic acid
DTI	Department of Trade and Industry
EFSA	European Food Safety Authority
EPSR	Engineering and Physical Sciences Research Council
ESBAC	Emerging Science and Bioethics Advisory Committee
ESRC	Economic and Social Research Council
FDA	(US) Food and Drug Administration
FET	Future Emerging Technologies
FSA	Food Standards Agency
GDP	Gross domestic product
GM	Genetically modified
GMO	Genetically modified organism
GNP	Gross national product
GSK	GlaxoSmithKline
HEFCE	Higher Education Funding Council for England
hESC	Human embryonic stem cell
HFEA	Human Fertilisation and Embryology Authority
HGC	Human Genetics Commission
HGP	Human Genome Project

HI	Health impact
HIF	Health impact fund
HIP	Health impact payment
ICT	Information and communications technologies
IPR	Intellectual property rights
IT	Information technologies
ITRS	International Technology Roadmap for Semiconductors
IVF	*In vitro* fertilisation
LMB	(Cambridge) Laboratory of Molecular Biology
MHRA	Medicines and Healthcare products Regulatory Agency
MoD	Ministry of Defence
MRC	Medical Research Council
NAS	New active substance
NEST	New and Emerging Science and Technologies
NHS	National Health Service
NSABB	(US) National Science Advisory Board for Biosecurity
OECD	Organisation for Economic Co-operation and Development
PPP	Public private partnerships
R&D	Research and development
REF	Research Excellence Framework
RNA	Ribonucleic acid
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property Rights
TSB	Technology Strategy Board
WHO	World Health Organization

Index

Locators point to paragraph or box numbers. Footnotes are indexed to the paragraph (or box) number that they relate to; some topics appear only in the footnotes.

Previous Nuffield Council Reports

Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review
Published June 2012

Human bodies: donation for medicine and research
Published October 2011

Biofuels: ethical issues
Published April 2011

Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age
Published October 2010

Dementia: ethical issues
Published October 2009

Public health: ethical issues
Published November 2007

The forensic use of bioinformation: ethical issues
Published September 2007

Critical care decisions in fetal and neonatal medicine: ethical issues
Published November 2006

Genetic Screening: a Supplement to the 1993 Report by the Nuffield Council on Bioethics
Published July 2006

The ethics of research involving animals
Published May 2005

The ethics of research related to healthcare in developing countries: a follow-up Discussion Paper
Published March 2005

The use of genetically modified crops in developing countries: a follow-up Discussion Paper
Published December 2003

Pharmacogenetics: ethical issues
Published September 2003

Genetics and human behaviour: the ethical context
Published October 2002

The ethics of patenting DNA: a discussion paper
Published July 2002

The ethics of research related to healthcare in developing countries
Published April 2002

Stem cell therapy: the ethical issues – a discussion paper
Published April 2000

The ethics of clinical research in developing countries: a discussion paper
Published October 1999

Genetically modified crops: the ethical and social issues
Published May 1999

Mental disorders and genetics: the ethical context
Published September 1998

Animal-to-human transplants: the ethics of xenotransplantation
Published March 1996

Human tissue: ethical and legal issues
Published April 1995

Genetic screening: ethical issues
Published December 1993

Published by
Nuffield Council on Bioethics
28 Bedford Square
London WC1B 3JS

Printed in the UK

ISBN 978-1-904384-27-4