Developing Facilitative Governance Frameworks for Emerging Biotechnologies: exploring new approaches to cross-border regulation

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ABSTRACT

The University of Manchester

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This thesis considers the applicability of 'new governance' techniques within the field of emerging biotechnologies. Through three contrasting case studies I construct an argument in favour of new governance, contending that the qualities of this regulatory trend (flexibility, reflexivity, nuance, open discourse, and participation – 'regulatory desirables') have much to offer the regulation of emerging biotechnologies.

The first case study examines the existing European and international regulatory frameworks for genetically modified organisms (GMOs). This case study explores the role of (bio)ethics within the regulatory process through each progressive stage: design, operation, and assessment. The regime's failure to provide adequate space for ethical reflection, and the limited role of ethics throughout the regulatory process prompts a proposal for an alternative approach that recognizes the multiple contexts in which regulation operates, and is able to accommodate the socio-ethical nuances of the GMO products being assessed.

This case study analyses a traditionally structured regulatory framework. It exemplifies a number of qualities that I consider undesirable in the context of regulating biotechnologies: inflexibility, lack of reflexivity, lack of nuance within the regime, absence of ethical discussion, absence of participation from all interested/affected parties. In the second and third case studies I show how these 'regulatory undesirables' can be addressed through new governance techniques.

The second case study focuses on the international regulation of stem cell research; I propose developing a polycentric, principles-based regulation (PBR) regime. The third case study centres on the international governance of the gene synthesis industry; here I recommend adopting a risk-based regulation (RBR) approach. In both these fields, voluntary, interdisciplinary, international organisations have collaborated to produce guidelines, codes, protocols, standards, and statements addressing matters of practice. I argue that these 'soft law' documents form the ideal starting point for the development of more sophisticated regulatory regimes in both fields. Furthermore, I argue that the informal organisations producing these documents are, in certain instances, best placed to step into the role of 'regulator' due to their in-depth, inside knowledge of the field, and network. Thus, I collapse the regulator-regulatee distinction held in traditional, 'command and control' style systems, as these organisations typically include those who would traditionally be seen as the 'regulatee'. Each case study considers the nuances of context vis-à-vis the regulatory approach advocated.

I conclude by engaging in a comparative analysis of these three case studies, drawing out the qualities, characteristics and considerations that I regard as essential to the construction of responsible, facilitative governance frameworks across the field of emerging biotechnologies. I conclude that new governance is best suited to achieving these (aforementioned) 'regulatory desirables'.

DECLARATION

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

COPYRIGHT STATEMENT

For my parents

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Nishat Hyder read Law at The London School of Economics and Political Science (LSE), graduating in 2005 with an LL.B (Hons.). Upon receiving the Jules Thorn Scholarship from the Honourable Society of the Middle Temple, she undertook the Bar Vocational Course at BPP Law School and was subsequently Called to the Bar of England and Wales in October 2006.

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In January 2011 Nishat began studying for a Ph.D. in Medical Jurisprudence and Bioethics at the University of Manchester's Centre for Social Ethics and Policy and School of Law. She was awarded one of the School of Law's Graduate Teaching and Research Assistant Scholarships; this enabled her to develop her skill-set and experience beyond the confines of doctoral research (details below).

Nishat hopes to continue pursuing research into the legal and ethical aspects of regulating biotechnologies, as well as advancing an equally rewarding teaching career.

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Hyder N. & Harris J., 'The Criminal Law and Enhancement – None of the Law's Business?' In Alghrani A., Bennett R & Ost S (eds.), (*Bioethics, Medicine and the Criminal Law, Volume 1: The Criminal Law and Bioethical Conflict: Walking the Tightrope* (Cambridge University Press, 2013)

Writer, *BioNews* (2009 – present) [please see: www.bionews.org.uk for an archive of news articles]

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> Quigley M., Chan S., and Harris J., (eds*) Stem Cells: New Frontiers in Science and Ethics* (World Scientific, 2012)
>
> Seddon, T., Williams, L. and Ralphs, R. *Tough Choices* (Oxford University Press, 2012).

Author: a statement on behalf of the University of Manchester (Centre for Social Ethics and Policy, and Institute for Science Ethics and Innovation) in response to the Nuffield Council for Bioethics' consultation on emerging biotechnologies (2011)

CHAPTER I

Introducing contemporary approaches to regulating emerging biotechnologies

1.1 Introduction

The problem of how to regulate emerging biotechnologies is a permanent issue on the modern political agenda. The rate of scientific advancement in fields such as synthetic biology, stem cell research and genetics, is such that there is renewed interest in governance mechanisms. Around the world, the question of how best to regulate these new areas of scientific and medical research continues to receive attention on several fronts. During the writing of this thesis, in the United Kingdom, for example, The Nuffield Council on Bioethics published recommendations on the plethora of issues emerging biotechnologies provokes, including regulation.[1] Further, the regulatory structure of, among other things, medical research was reconsidered under the Public Bodies Act 2011. Most recently, Parliament consulted on, developed, and approved regulations on the use of mitochondrial replacement techniques,[2] to name but a few examples.

Over the past few decades regulatory theory has developed as a discipline in its own right, and as a discourse bearing significant political import; successive governments across the globe have been preoccupied with re-crafting their regulatory approach to harmonize with the political message of the day. And conversely, developments in regulatory theory have influenced how politicians and policy makers approach the task of governing. In this thesis I will seek to analyse certain strands within contemporary regulatory theory, namely, 'new governance', in the context of their applicability to the international regulation of emerging biotechnologies. In order to do so I undertake three case studies in regulation from across the field of emerging biotechnologies (genetically modified organisms (GMOs), stem cell research and synthetic biology), examining how particular regulatory approaches have fared in the past, and considering the types of new governance approaches that hold promise for the future.

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[1] Nuffield Council on Bioethics, 'Emerging Biotechnologies: Technology, Choice and the Public Good' (2012).

[2] Sandy Starr, 'House of Lords Gives Green Light to Mitochondrial Donation' (*BioNews*, 2 March 2015) <http://www.bionews.org.uk/page_500475.asp> accessed 17 March 2015.

Regulation spans many disciplines, principally: law, economics, politics, history and sociology. Whilst these various dimensions of regulation will not be ignored, the primary focus of this project will be on regulatory policy, and role of law as an instrument of regulatory policy. The secondary focus will be to elucidate the underlying ethics of contemporary regulatory approaches analysed, and tease out the ethical implications of developing a policy accordingly. It is not my aim here to form and recommend a specific set of policies. However, insofar as it is possible, I will attempt take account of real-time developments in policy and science.

The purpose of this opening chapter is to provide a rudimentary background and context to the contrasting case studies that follow, and that comprise the main body of this thesis. This chapter consists of four sections. The first section, entitled, 'Legal and Ethical Background' (1.2) outlines the development of the regulatory theories and mechanisms that I will be focussing on. This section will be necessarily descriptive. However, as I will be analysing and applying very specific methods of regulation to the field of biotechnology in my case studies, it is pragmatic to provide a clear overview of these regulatory methods at the outset. In the second and third sections, entitled 'Ethical Approach' (1.3) and 'Legal Approach' (1.4) respectively, I attempt to demonstrate the nexus between regulation and ethics, and regulation and law, and some of the difficulties therein. Finally, in section four I introduce the case studies undertaken (1.5) that comprise the body of this thesis.

1.2 Legal and ethical background

The past half-century has seen the development of new forms of regulation.[3] This is in large part due to external factors such as the development of sophisticated political systems; growth, complexity and innovation in economics; globalisation; and the rise of powerful new industries. All of this has propelled regulation to expand beyond traditional regimes of 'command and control'[4] (CAC), which were for the most part state-centred and rule-centred, to the more nuanced, decentred network of governance we see today. Thus, the emergence of a modern regulatory style: 'new governance'.

1.2.1 New governance

The term 'New Governance' is difficult to define with precision; it is fluid, still in the process of growth and refinement. Indeed, in the introduction to their edited collection of essays *Law and New Governance in the EU and US* Grainne de Búrca and Joanne Scott explain the concept at length. They begin by pointing out that 'the concept of new governance is by no means a settled one'[5] then proceed to explain that new governance is a collective term that refers to mechanisms and procedures operating outwith the purview of legal institutions imposing the classic regulatory practice of command and control. They explain further:

> 'The language of governance rather than government in itself signals a shift away from the monopoly of traditional politico-legal institutions, and implies either the involvement of actors other than classically governmental actors, or indeed the absence of any traditional framework of government, as is the case in the EU and in any trans-national context'.[6]

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[3] I adopt a broad definition of the term 'regulation', embracing numerous conceptualizations of this notion as identified in Robert Baldwin, Martin Cave and Martin Lodge, *Understanding Regulation: Theory, Strategy, and Practice* (Oxford University Press 2011) chapters 2–3. This encompasses this following: 'an identifiable and discrete mode of governmental activity'; 'sustained and focussed control exercised by a public agency over activities that are valued by a community'; 'a specific set of commands'; 'deliberate state influence'; 'all forms of social or economic influence'; and finally, as both a red light (restrictive) and green light (facilitative) concept. Simply put, I define regulation as attempting to change behaviour in order tackle a particular issue by using a particular tool, mechanism, practice or approach recognized within the academic discipline we know as 'regulation'.

[4] Ibid 106–7.

[5] Graínne de Búrca and Joanne Scott, 'Introduction: New Governance, Law and Constitutionalism' in Graínne de Búrca and Joanne Scott (eds), *Law and New Governance in the EU and the US* (Hart Publishing 2006) 2.

[6] Ibid.

New governance is still in many ways experimental. Despite this, not only have new governance practices developed discretely across a plethora of policy areas, practices have also been borrowed or shared across diverse policy domains by industrial and governmental institutions. Although the practices themselves are varied, de Búrca and Scott reiterate commonality across these practices:

> 'Yet in each case, the common features which have been identified involve a shift in emphasis away from command-and-control in favour of 'regulatory' approaches which are less rigid, less prescriptive, less committed to uniform outcomes, and less hierarchical in nature. What can be seen already in this preliminary description is that new governance – as is suggested by the name – tends to be identified primarily by comparison with what it is not, and by contrast with some conception of traditional or 'old' regulatory approaches.'[7]

Others explain it as follows (note the same emphasis on new governance as '*anti*-command and control'):

> 'Where regulatory goals have traditionally been pursued exclusively through statutory enactments, administrative regulation, and judicial enforcement, we now see new processes emerging which range from informal consultation to highly formalized systems that seek to affect behaviour but differ on many ways from traditional command and control regulation. These processes, which we will collectively label "new governance" may encourage experimentation; employ stakeholder participation to devise solutions; rely on broad framework agreements, flexible norms and revisable standards; and use benchmarks, indicators and peer review to ensure accountability.'[8]

So, there is no checklist of criteria to determine whether any given approach or mechanism is strictly new governance. Whilst there is debate over the use and utility of new governance, and in particular, the role of law (a topic I shall return to in section 1.4), what is established is the definite emergence of this regulatory trend.[9] In the afterword to a recent symposium on new governance, Lisa Alexander commented:

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[7] Ibid.

[8] David M Trubek and Louise G Trubek, 'New Governance and Legal Regulation: Complementarity, Rivalry, and Transformation' (2006) 13 Colum. J. Eur. L. 539, 541.

[9] Given new governance is a well established regulatory trend I will not provide a historical overview of the emergence of this movement; for such an overview please see: de Búrca and Scott (n 5); Trubek and Trubek (n 8); David M Trubek and Louise G Trubek, 'Hard and Soft Law in the Construction of Social Europe: The Role of the Open Method of Co-Ordination' (2005) 11 European Law Journal 343; Colin Scott, 'Regulation in the Age of Governance: The Rise of the Post Regulatory State' in Jacint Jordana and David Levi-Faur (eds), *The Politics of Regulation: Institutions and Regulatory Reforms for the Age of Governance* (Edward Elgar Publishing 2004); Joanne Scott and David M Trubek, 'Mind the Gap: Law and New

> 'New governance clearly encompasses familiar recent governance innovations such as privatization, devolution, decentralization, public-private partnerships, and stakeholder collaboration, yet new governance seems to be more than simply the sum of those innovations. While new governance has many monikers, and defies precise definition, there is a coherence underlying the broad range of scholarship in this Symposium that gives us a sense that "we know it when we see it."'[10]

Finally, new governance techniques have expanded beyond regulatory policy for business (in the strict sense) and begun to infiltrate general societal governance, globally.[11]

In this thesis I will be analysing closely two regulatory approaches that fall within the spectrum of new governance, namely, Principles-based Regulation (PBR)[12] and Risk-based Regulation (RBR)[13] and some mixed models involving either PBR or RBR, such as the integration of Really Responsive Regulation (RRR) with RBR, and a 'polycentric' PBR model. While these are only two of the plethora of new governance mechanisms available, a comprehensive assessment would be outside the scope of this project, and not all of the mechanisms are relevant or appropriate to regulation of emerging biotechnologies. (Explaining and justifying why I believe PBR and RBR are relevant to this field will form an important part of my analysis as this thesis progresses.) What follows is a brief account of these approaches, and the political context in which they arose. However it is important to bear in mind that these theories are still in the process of being developed and must be seen against the backdrop of the 'better regulation' and 'smart regulation' movements, rather than discrete strategies, unaffected by government policy.

Approaches to Governance in the European Union' (2002) 8 European Law Journal 1; Grainne De Burca, 'The Constitutional Challenge of New Governance in the European Union' (2003) 28 European Law Review 814; Cristie L Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (2008) 45 American Business Law Journal 1; Orly Lobel, 'Renew Deal: The Fall of Regulation and the Rise of Governance in Contemporary Legal Thought, The' (2004) 89 Minn. L. Rev. 342; Charles F Sabel and Jonathan Zeitlin, 'Learning from Difference: The New Architecture of Experimentalist Governance in the EU' (2008) 14 European Law Journal 271.

[10] Lisa T Alexander, 'Reflections on Success and Failure in New Governance and the Role of the Lawyer' (2010) 2010 Wisconsin Law Review 737, 739.

[11] 'Governing Societies: The Emergence of New Governance Structures' *The Trinidad Guardian Newspaper* (1 April 2011) <http://www.guardian.co.tt/business-guardian/2011/03/31/governing-societies-emergence-new-governance-structures> accessed 23 March 2015.

[12] See 1.2.4 and chapter III

[13] See 1.2.5 and chapter IV

1.2.2 Better regulation

In 1997 newly elected New Labour government created the Better Regulation Task Force; its task was to advise the government on crafting 'better regulation'. The Task Force identified five principles of good regulation, which should be:

- transparent
- accountable
- proportionate
- consistent
- targeted – only at cases where action is needed[14]

These five principles continue to inform the regulatory agenda in the UK. They are enshrined in legislation[15] and implemented through the Regulators' Code[16] and the Better Regulation Framework Manual.[17] In the UK the Better Regulation agenda is overseen by the Better Regulation Executive,[18] Better Regulation Delivery Office,[19] and Regulatory Policy Committee,[20] under the purview of the Department for Business Innovation and Skills.[21]

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[14] Better Regulation Task Force, 'Principles of Good Regulation' (2003) <http://webarchive.nationalarchives.gov.uk/20100407162704/http:/archive.cabinetoffice.gov.uk/brc/upload/assets/www.brc.gov.uk/principlesleaflet.pdf> accessed 30 March 2015; Better Regulation Task Force, 'Better Regulation - from Design to Delivery' (2005) Annual Report <http://www.eesc.europa.eu/resources/docs/designdelivery.pdf> accessed 30 March 2015; OECD, 'Better Regulation in Europe: United Kingdom' (2010) <http://www.oecd.org/regreform/regulatory-policy/44912232.pdf> accessed 30 March 2015; 'The Five Principles of Good Regulation' (*Department for Business Innovation & Skills*, 6 March 2012) <http://webarchive.nationalarchives.gov.uk/20121212135622/http://www.bis.gov.uk/policies/bre/policy/five-principles-of-good-regulation> accessed 23 March 2015; 'Better Regulation' (*Department for Business Innovation & Skills*, 9 April 2010) <http://webarchive.nationalarchives.gov.uk/20090609003228/http://www.berr.gov.uk/policies/better-regulation> accessed 23 March 2015.

[15] Legislative and Regulatory Reform Act 2006 s.21(2).

[16] Better Regulation Delivery Office, *Regulators Code* (2014) s.1.4 <https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/300126/14-705-regulators-code.pdf> accessed 30 March 2015.

[17] Department for Business Innovation & Skills, *Better Regulation Framework Manual* (2015) p.4 <https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/211981/bis-13-1038-better-regulation-framework-manual-guidance-for-officials.pdf> accessed 30 March 2015.

[18] 'Better Regulation Executive' (*GOV.UK*) <https://www.gov.uk/government/groups/better-regulation-executive> accessed 31 March 2015.

[19] 'Better Regulation Delivery Office' (*GOV.UK*) <https://www.gov.uk/government/organisations/better-regulation-delivery-office> accessed 31 March 2015.

[20] 'Regulatory Policy Committee' (*GOV.UK*) <https://www.gov.uk/government/organisations/regulatory-policy-committee> accessed 31 March 2015.

[21] The Better Regulation Delivery Office replaced the local Better Regulation Office in 2011. The Better Regulation Executive is what remains of the Better Regulation Task Force and the many guises it has taken since. The Better Regulation Task Force was replaced in 2006 by the Better Regulation Commission, which itself was subsequently abolished in 2008. The Commission was replaced by the short-lived Risk and Regulatory Advisory Council, which was abolished in 2009. The Better Regulation

The concept of 'better regulation' has expanded and developed, most notably by Sir Philip Hampton's review of 2005. The Hampton Review investigated how to reduce the administrative burden of regulation, without compromising regulatory goals;[22] government subsequently adopted the recommendations put forward in the Hampton Review.[23] In addition to a number of specific recommendations the Review laid out several principles:

- regulators, and the regulatory system as a whole, should use comprehensive risk assessment to concentrate resources on the areas that need them most;
- regulators should be accountable for the efficiency and effectiveness of their activities, while remaining independent in the decisions they take;
- no inspection should take place without a reason;
- businesses should not have to give unnecessary information, nor give the same piece of information twice [to the regulator];
- the few businesses that persistently break regulations should be identified quickly and face proportionate and meaningful sanctions;
- regulators should provide authoritative, accessible advice easily and cheaply;
- regulators should be of the right size and scope, and no new regulator should be created where an existing one can do the work; and
- regulators should recognize that a key element of their activity will be to allow, or even encourage, economic progress and only to intervene when there is a clear case for protection.[24]

Executive was established following the 2005 Hampton Report. It replaced the Regulatory Impact Unit, which used to support the old Better Regulation Task Force. I have provided a brief history of the structural changes in government that resulted in the current BRE and BRDO. For a more detailed account please see: 'The Regulatory Burden: Getting the Balance Right' (*Policy@Manchester*) <http://www.policy.manchester.ac.uk/resources/regulation/balance/> accessed 23 March 2015.

[22] Philip Hampton, 'Reducing Administrative Burdens: Effective Inspection and Enforcement' (HM Treasury 2005) <http://webarchive.nationalarchives.gov.uk/20090609003228/http://www.berr.gov.uk/files/file22988.pdf> accessed 30 March 2015.

[23] See the government's official response to the Hampton Review: HM Treasury, Better Regulation Executive and Cabinet Office, 'Implementing Hampton: From Enforcement to Compliance' (2006) <http://webarchive.nationalarchives.gov.uk/+/http://www.hm-treasury.gov.uk/d/hampton_compliance281106.pdf> accessed 23 March 2015.

[24] Hampton (n 22) 7.

In 2006 a report was commissioned from Richard Macrory to advise to how to improve regulatory compliance.[25] The Macrory Report follows on from the Hampton Report and the BRTF's principles of good regulation. Importantly, the Report set out six penalty principles that seek to guide the design and implementation of sanctions within a regulatory regime. Thus, a sanction should:

1. Aim to change the behaviour of the offender;
2. Aim to eliminate any financial gain or benefit from non-compliance;
3. Be responsive and consider what is appropriate for the particular offender and regulatory issue, which can include punishment and the public stigma that should be associated with a criminal conviction;
4. Be proportionate to the nature of the offence and the harm caused;
5. Aim to restore the harm caused by regulatory non-compliance, where appropriate; and
6. Aim to deter future non-compliance.[26]

The recommendations of the Macrory Report (which were accepted by the government, and implemented through the enactment of the Regulatory Enforcement and Sanctions Act 2008) together with the recommendations of the Hampton Review, and the key principles identified in both reports continue to influence governmental agenda on achieving better regulation.

The principles that have emerged from the Better Regulation movement are not sector-specific; their application to regulating emerging biotechnologies is not unique. I have outlined this movement in order to provide some background to the government-mandated principles of regulation that affect *all* regulatory regimes in the United Kingdom, including biotechnology.

1.2.3 Smart regulation

'Smart regulation' was developed by Gunningham and Grabosky; the concept was laid out in their seminal work, *Smart Regulation: Designing Environmental Policy*.[27] In essence smart regulation argues that:

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[25] Richard Macrory, 'Regulatory Justice: Making Sanctions Effective: Final Report' (Cabinet Office 2006) <http://webarchive.nationalarchives.gov.uk/20070305103615/http:/cabinetoffice.gov.uk/regulation/reviewing_regulation/penalties/index.asp> accessed 30 March 2015.
[26] Ibid 12.
[27] Neil Gunningham, Peter N Grabosky and Darren Sinclair, *Smart Regulation: Designing Environmental Policy* (Clarendon Press 1998).

> '…in the majority of circumstances, the use of multiple rather than single policy instruments, and a broader range of regulatory actors, will produce better regulation. Further, that this will allow the implementation of complementary combinations of instruments and participants tailored to meet the imperatives of specific [issues].'[28]

Smart regulation means:

> '…to include not just conventional forms of direct ("command and control") regulation but also to include much more flexible, imaginative and innovative forms of social control which seek to harness not just governments but also business and third parties. For example, we are concerned with self-regulation and co-regulation, with utilising both commercial interests and Non-Government Organisations, and with finding surrogates for direct government regulation, as well as with improving the effectiveness and efficiency of more conventional forms of direct government regulation.'[29]

Exploiting an assortment of techniques and actors within the regulatory landscape involves embracing a greater degree of communication and co-operation between both the actors and various policy-instruments. A smart regulation system is pluralistic and multi-level. This approach has been adopted and developed by institutions such as the Organisation for Economic Co-operation and Development (OECD)[30] and European Commission.[31]

In October 2010 the OECD held its first conference on regulatory policy, in partnership with the European Commission.[32] The conference report explains smart regulation as follows:

> 'Smart regulation doesn't just look at the quality of new proposals through impact assessments. It takes into account the whole policy cycle – from rationale to adoption of the design, implementation, and monitoring ex post.'[33]

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[28] Ibid 4.
[29] Neil Gunningham and Darren Sinclair, 'Designing Smart Regulation' in Bridget M Hutter (ed), *A Reader in Environmental Law* (Oxford University Press 1999) 305.
[30] Viola Groebner, 'Guiding the Road to Recovery and Growth', *Regulatory Policy at the Crossroads - Towards a new Policy Agenda* (OECD 2010) <http://www.oecd.org/regreform/policyconference/46428369.pdf> accessed 23 March 2015.
[31] Ibid.
[32] OECD, 'Regulatory Policy: Towards a New Agenda' (2010) <http://www.oecd.org/gov/regulatory-policy/47298590.pdf> accessed 23 March 2015.
[33] Ibid 10.

Interestingly, the conference report also highlighted the organising institutions' commitment to better regulation, and move towards integrating better regulation with a smart regulation approach:

> 'The European Commission has switched from better regulation to Smart regulation – and it's not just a word. In the past, 'better' focused on the quality of new proposals, with impact assessments. 'Smart' recognises that while better regulation has an important role to play in achieving a better life for citizens and a better environment for businesses, we need to get it right. Smart regulation now looks at the whole circle, recognising that legislative proposals reflect the revision and improvement of existing legislation.'[34]

Better and smart regulation approaches are not mutually exclusive; the move to integrate the two has prompted some commentators to note the tension between the two:

> 'Better regulation had not yet achieved its full impact… In this context the innovations introduced by smart regulation can be welcome if they do not undermine or slow down the sustained delivery of ongoing better regulation results.'[35]

Writers in the field of Science and Technology Studies such as Sheila Jasanoff have emphasised the weight of political power held by 'Science' today.[36] The biotechnology sector is immensely complex and devising one single policy instrument to regulate the behaviour and input of all relevant parties (which include pharmaceutical companies, publicly-funded research facilities, private research facilities, lobby groups, patient groups and the medical profession to name a few) is a difficult, ambitious task. Given this, I submit that dispersing the task of regulating a) between a number of appropriate political and industrial institutions, and b) using a number of appropriate approaches and tools, makes sense. In other words, following the philosophy of smart regulation. A multiple-angle approach rather than a single, linear attempt at comprehensive regulation will enable a nuanced approach to the myriad issues posed by each strand of biotechnological development. Accordingly, in chapters III and IV I develop my

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[34] Ibid 11. (Quoting Marianne Klingbeil, Director for Better Regulation; Acting Chair of the Impact Assessment Board, Secretariat-General, European Commission)

[35] Charles-Henri Montin, 'Smart Regulation in the European Union' (*Smart Regulation*, 8 October 2010) 23 <http://montin.com/archive/documents/smartregulation.pdf> accessed 23 March 2015.

[36] Sheila Jasanoff, *The Fifth Branch: Science Advisers as Policymakers* (Harvard University Press 1994); Sheila Jasanoff, *Designs on Nature: Science and Democracy in Europe and the United States* (Princeton University Press 2011).

proposals for the international stem cell research, and international gene synthesis industry further.[37]

Against the backdrop of these movements that have impacted upon regulatory policy at both national and international levels, more specific approaches such as PBR and RBR have developed. It is to these approaches I now turn my attention.

1.2.4 Principles-based regulation[38]

The use of principles (as opposed to rules) in law is of course, by no means a new initiative,[39] however the recent development and recognition of a specific, principles-based approach to regulation is a contemporary trend that is of interest. Much has been written about PBR following the global financial crisis: in the UK the crisis was seen to indicate a failure of PBR,[40] whereas as in the USA it was the reverse, a failure of rules-based regulation and a prompt towards PBR. The rules-versus-principles debate continues and both approaches have strengths and weaknesses; but this debate is much more than an academic quibble. As Julia Black says,

> 'The question of when to use rules, principles, or standards has also become a policy issue in its own right. In some policy areas, though by no means all, they have been recognised as being particular 'technologies' of regulation and as having particular properties, properties which policymakers in some areas have consciously sought to use and exploit for a variety of ends.'[41]

She continues:

> 'These monikers are more than just descriptions, however; they also carry significant normative content. Being 'rules-based' is usually denigrated as

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[37] See also 5.3 on selecting appropriate regulatory tools and approaches.

[38] See chapter III

[39] For example, in Common Law jurisdictions principles or doctrines set out by judges in their judgments are an important source of law. A principle will declare a standard in general terms; it is then subject to subsequent explanation, refinement and qualification through interpretation and the application of legal tests. Furthermore, in contemporary jurisprudence Ronald Dworkin's explanation of law relies on a rules/principles distinction (although the definition and operation of 'rules' and 'principles' will differ according to context, I submit that the analogy still bears some relevance). See: Ronald M Dworkin, 'The Model of Rules' [1967] The University of Chicago Law Review 14; John Braithwaite, 'Rules and Principles: A Theory of Legal Certainty' (2002) 27 Australian Journal of Legal Philosophy 47.

[40] The Financial Services Authority (FSA) was one of the most vocal proponents of PBR, and seen worldwide as a 'leader' crafting PBR for financial services industry. Julia Black, 'Paradoxes and Failures: "New Governance" Techniques and the Financial Crisis' (2012) 75 The Modern Law Review 1037; Julia Black, 'Forms and Paradoxes of Principles-Based Regulation' (2008) 3 Capital Markets Law Journal 425; Julia Black, 'The Rise, Fall and Fate of Principles Based Regulation' [2010] LSE Legal Studies Working Paper No.17/2010; Julia Black, Martyn Hopper and Christa Band, 'Making a Success of Principles-Based Regulation' (2007) 1 Law and Financial Markets Review 191.

[41] Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40) 2.

> equating with nit-picking bureaucracy in which compliance with detailed provisions is more important than the attainment of an overall outcome. 'Principles-based', in contrast, evokes images of outcome orientated, flexible regulators harbouring ethical standards in largely responsible corporations.'[42]

Much has been written about the pros and cons of rules-based and principles-based systems (and indeed further alternatives): rules lend certainty, principles allow for flexibility, but then, rules are inflexible, principles lead to uncertainty. I do not propose to delve into this debate here as it is well documented in the regulatory literature.[43]

So what exactly is PBR? Julia Black, who has contributed significantly to the development of contemporary PBR in both theory and practice (certainly in the United Kingdom), characterizes PBR as two-dimensional. Firstly, a PBR regime can be either formal/rule-book or substantive (or indeed both). Secondly, the institutional setting of the regime can be either dyadic or polycentric. She summarises these dimensions thus:

> 'PBR can be formal, in the sense that there are principles in the rulebooks (including legislation, codes of practice and so on) but it may not be substantive. In contrast, a regime may have some of the operational characteristics of a PBR regime, but not have principles in the rulebooks. Where it is both, it is described as full PBR. Polycentric PBR is full PBR with the additional element that it is characterized by the enrolment of others, beyond regulators and firms, in the elaboration of the meaning and application of principles…These labels are not intended to have normative overtones; they are simply useful shorthand descriptions.'[44]

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[42] Ibid 3.

[43] However, in putting forward my arguments throughout this thesis I will, where necessary, address the arguments. For an overview of the rules versus principles debate please see the following: Anita I Anand, 'Rules v. Principles as Approaches to Financial Market Regulation' (2008) 49 Harvard International Law Journal <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2340670> accessed 30 March 2015; Robert Baldwin, 'Why Rules Don't Work' (1990) 53 The Modern Law Review 321; Julia Black, *Rules and Regulators* (Oxford University Press 1997); Black, Hopper and Band (n 40); Julia M Black, '" Which Arrow?": Rule Type and Regulatory Policy' [1995] Public Law 94; Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Braithwaite, 'Rules and Principles' (n 39); Lawrence A Cunningham, 'Prescription to Retire the Rhetoric of Principles-Based Systems in Corporate Law, Securities Regulation, and Accounting, A' (2007) 60 Vand. L. Rev. 1409; Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Louis Kaplow, 'Rules versus Standards: An Economic Analysis' (1992) 42 Duke Lj 557; Russell B Korobkin, 'Behavioral Analysis and Legal Form: Rules vs. Principles Revisited"(2000)' 79 Or. L. Rev. 23; Eric A Posner, 'Standards, Rules, and Social Norms' (1997) 21 Harv. JL & Pub. Pol'y 101; Frederick Schauer, 'Convergence of Rules and Standards, The' [2003] NZL Rev. 303; Frederick Schauer, 'Tyranny of Choice and the Rulification of Standards, The' (2004) 14 J. Contemp. Legal Issues 803; Cass R Sunstein, 'Problems with Rules' [1995] California Law Review 953.

[44] Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40) 428.

The central criticism of PBR is that of uncertainty. An extract from the Legal Week blog sums demonstrates the difficulty of PBR simply:

> 'Let me close with a more homespun example. On a Saturday morning, your correspondent is often to be found wandering the aisles of his local supermarket, carefully studying a list of items provided to him by Mrs K. In a 'principles-based' world, the list would probably contain something like this: "(i) Buy things which are healthy. (ii) Buy things the kids like. (iii) Look out for special offers. (iv) Find things which are high in fibre. (v) Consider the welfare of the chickens that laid the eggs" or similar. Make up your own list. If I had a principles-based shopping list, who knows what I'd actually decide to buy?
>
> On the other hand, a rules-based shopping list would probably say "Buy 12 medium eggs". Much easier to know what to do. But if I didn't know that our household favours free range as a matter of principle, I could also buy the wrong thing.'[45]

However, the criticisms of PBR are not all based on the principles-rules dichotomy, PBR can be criticised on its own terms. Black identifies seven paradoxes of PBR that might be summarized as follows. The first is that principles are purposely framed in imprecise terms to give both regulator and regulatee flexibility. However, a principle might be interpreted a) in precise terms and b) in different terms by different parties, all of which will lead to confusion and conflict. The second paradox is that although one of the advantages of PBR is that it can facilitate communication between parties, the regulator might be tempted into issuing an overwhelming amount of guidance (even with the best of intentions), thereby abolishing scope for communication. Thirdly, regulatees might not take advantage of the flexibility principles provide (continuing to act in a conservative, uniform manner), for fear of misinterpreting the principle and attracting sanctions. In the aftermath of the global banking crisis, *New Yorker* journalist James Suroweicki wrote:

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[45] Tom Kilroy, 'Principles-Based Regulation - Let's Not Do That Again' (*LegalWeek*, 10 March 2011) <http://www.legalweek.com/legal-week/blog-post/2032965/principles-regulation> accessed 24 March 2015. Of course, the rules-based list could simply read 'Buy 12 medium *free-range* eggs' but that would be to miss the point. Besides, indicating the appropriate level of detail for a smooth grocery run is one matter, governing complex financial transactions is quite another.

> 'A principles-based system offers the potential for smarter regulation—the kind that helps markets work more efficiently. But the best principles in the world won't help much if those in charge aren't willing to enforce them.'[46]

Indeed, enforcement is necessary to establish credibility, yet over-enforcement would defeat the spirit and purpose of PBR – and this is the fourth paradox. The fifth paradox is that the flexibility (supposedly a positive thing) that PBR provides internal management can become burdensome. Detailed rules give internal management the clout and credibility to direct their organisations behaviour – under PBR this is much more difficult. Sixthly, the ethical paradox is that although PBR gives firms the opportunity to take account of ethics when making business decisions, it also opens up the possibility that firms might make the wrong or unethical decision. Finally, PBR can help build qualities such as trust and responsibility within the regulatory regime, but even the simplest understanding of PBR shows that these qualities need to be present in the first place for PBR to operate successfully. As Hector Sants, Chief Executive of the FSA, aptly commented: '[A] principles-based approach does not work with individuals who have no principles.'[47]

Despite the battering PBR has taken post-banking crisis, it remains a relatively strong contender amongst the various forms of regulation available to designers.[48] Although the UK Financial Services Authority has distanced itself from PBR, rebranding its approach 'outcomes-based' regulation (notwithstanding the public rebrand, little has changed on paper, for example, the FSA's principles of business remain intact)[49] others are turning towards PBR now. Financial regulators in Japan and America are integrating PBR into their respective regimes,[50] and the Legal Services Board and Solicitors Regulation Authority in the UK have both opted for PBR.[51] Most pertinently for this

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[46] James Surowiecki, 'Parsing Paulson' [2008] *The New Yorker* <http://www.newyorker.com/magazine/2008/04/28/parsing-paulson> accessed 24 March 2015.

[47] 'Delivering Intensive Supervision and Credible Deterrence: Speech by Hector Sants, Chief Executive, FSA The Reuters Newsmakers Event' (*FSA*, 12 March 2009) <http://www.fsa.gov.uk/pages/Library/Communication/Speeches/2009/0312_hs.shtml> accessed 24 March 2015.

[48] Black, 'Paradoxes and Failures' (n 40).

[49] Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40) 13; Financial Services Authority, 'A Regulatory Response to the Global Banking Crisis' (2009) Discussion Paper 09/2 <http://www.fsa.gov.uk/pubs/discussion/dp09_02.pdf> accessed 30 March 2015.

[50] Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40) 3.

[51] Ibid; Legal Services Board, 'Business Plan 2009/10' (2009) <http://www.legalservicesboard.org.uk/news_publications/publications/pdf/business_plan_2009_10.pdf> accessed 1 April 2015; Solicitors Regulation Authority, 'Achieving the Right Outcomes - Closed Consultation' (2010) <http://www.sra.org.uk/consultations/achieving-right-outcomes/> accessed 1 April 2015.

project, the Human Fertilisation and Embryology Authority (hereafter HFEA) has adopted PBR as part of its regulatory regime[52] and PBR is the approach of choice for developing a voluntary Code of Conduct for research in nanotechnology.[53] The great attraction PBR holds for the field of biotechnology is the flexibility it affords both the regulator and regulate. Given the speed of scientific advance – which by far outstrips the speed of the legislative process – flexibility is key to effective, on-going regulation of current activity. For example, technology to create human-animal admixed embryos was established long before Parliament enacted legislation to regulate this technique. The Human Fertilisation and Embryology Act 2008[54] was passed 'after the event' in order to regulate *inter alia* the creation and use of human-animal admixed embryos for research purposes. PBR as an adaptive mechanism will, I submit, go some way towards addressing the regulatory 'lag' that often occurs in regulating biotechnologies. I will return to look at these examples in the forthcoming sections and chapters.

1.2.5 Risk-based regulation[55]

Risk-based regulation has become an increasingly popular method of governance in public and private institutions. Following the banking crisis, risk-based regulation and compliance has come under the spotlight,[56] escalating the public visibility of this technique. Like PBR, RBR is not a particularly new approach – it is merely in current vogue.[57]

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[52] Human Fertilisation and Embryology Authority, *HFEA - Code of Practice 8th Edition* (2009) <http://www.hfea.gov.uk/code.html> accessed 1 April 2015.
Very little has been written on the HFEA's adoption of PBR, however see: Sarah Devaney, 'Regulate To Innovate: Principles-Based Regulation of Stem Cell Research' (2011) 11 Medical Law International 53; Sarah Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (Routledge 2014).

[53] Insight Investment, Royal Society, Centre for Process Innovation, Nanotechnology Industries Association, *The Responsible Nano Code* (2008) <http://www.nanoandme.org/downloads/The%20Responsible%20Nano%20Code.pdf> accessed 1 April 2015.

[54] Human Fertilisation and Embryology Act 2008.

[55] See chapter IV

[56] Black, 'Paradoxes and Failures' (n 40).

[57] It is important to clarify that although similar and parallel narratives of risk-based regulation may be found in other jurisdictions around the world, I draw specifically on Black and Baldwin's depiction of RBR whose work has been largely shaped by the UK experience. See: Julia Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' [2005] Public law 512; Julia Black, 'The Role of Risk in Regulatory Processes' in Robert Baldwin, Martin Cave and Martin Lodge (eds), *The Oxford Handbook of Regulation* (Oxford University Press 2010); Julia Black and Robert Baldwin, 'When Risk-Based Regulation Aims Low: Approaches and Challenges' (2012) 6 Regulation & governance 2; Julia Black and Robert Baldwin, 'Really Responsive Risk-Based Regulation' (2010) 32 Law & Policy 181; Julia Black, 'Risk-Based Regulation: Choices, Practices and Lessons Being Learned' in OECD (ed), *Risk and Regulatory Policy: Improving the Governance of Risk* (OECD 2010).
See also: Bridget M Hutter, *The Attractions of Risk-Based Regulation: Accounting for the Emergence of Risk Ideas in Regulation* (Discussion Paper 33/2005, Centre for Analysis of Risk and Regulation, London School of

RBR developed in response to the over-saturation of inflexible, regulation resulting in inefficient, ineffective and expensive practices that came to characterize the worst of the 'regulatory state'.[58] In the United Kingdom, for example, contemporary RBR is equally a product of the political climate, and motivations and shifts within regulatory discourse: the 'new public management' movement that swept through public administration in the 1980's,[59] and the Better Regulation trend beginning in the late 1990's.[60] The Hampton Review[61] of 2005 elaborated on the original principles of Better Regulation to specifically incorporate risk-based approaches. Subsequently, under the statutory Regulators' Compliance Code,[62] which was based on the Hampton Principles, and its recent replacement, the Regulators' Code,[63] all UK regulators are required to take account of risk as part of their regime: 'regulators, and the regulatory system as a whole, should use comprehensive risk assessment to concentrate resources on the areas that need them most'.[64]

These shifts in regulatory style were accompanied by powerful and compelling political rhetoric, which encouraged the flourishing of new (risk-based) practices; in particular, the UK's FSA has contributed significantly to the development and practice of RBR.[65] And, despite it's bruised reputation post-banking crisis, RBR remains a key component of the regulatory framework of a plethora of organisations, public and private, across numerous industries, including the banking sector.[66] In the field of medical

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Economics and Political Science 2005); Bridget M Hutter, 'Risk, Regulation, and Management' in Peter Taylor-Gooby and Jens O Zinn (eds), *Risk in Social Science* (Oxford University Press 2006).

[58] Hutter, *The Attractions of Risk-Based Regulation* (n 57); Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).

[59] In Britain the government introduced a set of changes that we now term 'new public management', aimed at modernizing public administration, reducing the regulatory burden and costs, improving efficiency and clarity, through *inter alia* borrowing regulatory techniques from the private sector: Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57); Christopher Hood, 'A Public Management for All Seasons?' (1991) 69 Public Administration 3.

[60] Better Regulation Task Force, 'Principles of Good Regulation' (n 14); Better Regulation Task Force, 'Better Regulation - from Design to Delivery' (n 14); OECD (n 14); 'The Five Principles of Good Regulation' (n 14); 'Better Regulation' (n 14). See 1.2.2
See also: 1.2.2

[61] Hampton (n 22).

[62] Better Regulation Executive, *Regulators' Compliance Code: Statutory Code of Practice for Regulators* (2007) <http://webarchive.nationalarchives.gov.uk/20090609003228/http://www.berr.gov.uk/files/file45019.pdf> accessed 24 March 2015.

[63] Better Regulation Delivery Office (n 16).

[64] Hampton (n 22) 13.

[65] Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).

[66] Black, 'Paradoxes and Failures' (n 40).

technologies, for example, the HFEA is developing and fine-tuning its risk-based management approach.[67]

An RBR approach involves assessing how much risk an institution can absorb and manage:

> 'At its simplest, risk based regulation can be conceived as allocating resources in proportion to risks to society (such as health, safety or environmental risks), considering both the impacts themselves and the likelihood that they happen, in order to establish appropriate levels of control…
>
> 'Risk-based regulation…is often additionally conceived as the assessment and management of the bundle of issues usually termed 'business risks' associated with delivering regulatory objectives and we would expect good practice approaches to be thus characterised.'[68]

It is essentially a method of resource allocation, in which risks are prioritized and targeted accordingly.[69] Under RBR, organisations are *expected* to fail to achieve their objectives to some extent; RBR allows the organisation to cope with that failure. Defining what counts as a risk is tricky:

> 'Risk' is conventionally conceived as a concern both with potential impact (both positive and negative) and the probability of impacts occurring (Gratt 1987). But beyond that, there is little agreement about what kinds of risks come within the ambit of governance or how they should do so.'[70]

In the quote above, Rothstein et al distinguish between two broad types of risk, societal risk and institutional risk, which are helpful and well-known labels.[71] However, more specific categorisation of risk is likely to be controversial. Tools of RBR are numerous

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[67] Better Regulation Executive, 'Human Fertilisation and Embryology Authority: Hampton Implementation Review Report' (2009) <http://webarchive.nationalarchives.gov.uk/20121212135622/http://www.bis.gov.uk/files/file53852.pdf> accessed 24 March 2015; Human Fertilisation and Embryology Authority, 'Human Fertilisation and Embryology Authority: Annual Report and Accounts 2009/10' (2010) HC 32 <http://www.hfea.gov.uk/docs/Annual_Report_2010_Web_reduced.pdf> accessed 24 March 2015.

[68] Henry Rothstein and others, 'The Risks of Risk-Based Regulation: Insights from the Environmental Policy Domain' (2006) 32 Environment International 1056, 1057.

[69] Black and Baldwin, 'When Risk-Based Regulation Aims Low' (n 57); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Black, 'The Role of Risk in Regulatory Processes' (n 57).

[70] Henry Rothstein, Michael Huber and George Gaskell, 'A Theory of Risk Colonization: The Spiralling Regulatory Logics of Societal and Institutional Risk' (2006) 35 Economy and Society 91, 92.

[71] The same distinction is made by Black in: Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).

and varied, but contain at a minimum the hybrid approach of scientific risk assessment plus economic cost-benefit analysis.[72]

So, why opt for RBR? RBR by definition places risk at the heart of the regulatory model, forcing organisations to think about issues that might otherwise be overlooked and/or poorly managed. Resources are finite and one of the advantages of RBR is that it is a method of resource management; resources are targeted and used proportionately promoting efficiency. RBR also provides a decision-making rationale, which will appeal to pragmatic managers:

> 'Risk-based decision-making provides one way of managing institutional risks by explicitly anticipating those risks within probabilistic calculations of regulatory success and failure (cf. Luhmann, 1993; Rothstein et al., 2006). Conceived in this way, risk-based regulation is about defining the limits of what regulation can be expected to achieve. Risk is therefore an attractive concept for regulators because it provides a powerful rationale for regulatory activity and behaviours.'[73]

The scientific evidence-base that underlies RBR lends decisions made under this approach the cachet of objectivity, and therefore helps legitimate the regulatory model.[74] In addition, RBR limits the boundaries of accountability and responsibility and is therefore attractive to regulators.[75] Finally, RBR is thought to be a good tool to combat 'regulatory creep' (that is to say, the gradual expansion and escalation of regulatory control beyond the original regulatory remit), and the associated lack of flexibility.[76]

RBR is not without its own set of risks. Firstly, RBR attempts to use methods of scientific analysis (i.e. evidence base) to determine risk, but by its very nature, risk is unquantifiable – at least, it is often not possible to quantify risk with the degree of precision that regulators and managers desire. Secondly, risk-based decision-making might conflict normatively with pre-existing decision making strategies causing internal institutional problems. Finally, following a risk-based decision making strategy might lead to decisions that are unpalatable, either to the institution itself, or to stakeholders and partner institutions.[77] For example, a risk-based strategy might advocate absorbing

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[72] Hutter, *The Attractions of Risk-Based Regulation* (n 57).
[73] Rothstein and others (n 68) 1057.
[74] Hutter, *The Attractions of Risk-Based Regulation* (n 57).
[75] Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).
[76] Ibid; Hutter, *The Attractions of Risk-Based Regulation* (n 57).
[77] Rothstein and others (n 68).

certain risks on grounds of pragmatism, which may conflict with a company's Corporate Social Responsibility agenda. So, there is potential for tension between managing societal and institutional risk, which in turn will cause confusion in assessing regulation itself, and achieving regulatory goals. A further criticism of RBR is the potential to i) over-emphasise risk itself, and ii) unnecessarily amplify certain risks. The temptation is, as Power pithily puts it, to be preoccupied with the 'risk management of everything'.[78] Finally, Rothstein et al put forward an arguably more potent worry in their 'theory of risk colonization':

> 'Constructing regulatory objects in terms of risk, however, provides a defensible procedural rationality for regulators to manage both their regulatory objects and their enhanced institutional threats. We argue that this reflexive aspect of risk governance can lead to a phenomenon of 'risk colonisation', whereby risk increasingly comes to define the object, methods and rationale of regulation…'risk colonisation' can have a spiralling tendency where mismatches between the management of societal and institutional risk drive regulators to ever further activity.'[79]

Despite the risks and disadvantages of RBR, the approach may still prove useful in designing regulatory regimes for 'risky' technologies. For example, the risks associated with synthetic biology are often cited as the greater concern than the actual technology itself (processes) or what it is trying to achieve (products). Therefore, focussing on risk when designing a regulatory regime for synthetic biology might be a more beneficial approach than traditional approaches that focus on controls and procedures (although recall that in the UK, at least, following the Hampton Review all regulators must undertake appropriate risk assessments). I am not suggesting that RBR alone can effectively regulate a technology such as synthetic biology however in chapter IV I develop the argument that RBR ought to play a greater role than it currently does in regulating research in synthetic biology.

RBR is used in conjunction with other regulatory approaches. One such mixed model combines RBR and meta-regulation,[80] and another commingles RBR and Really

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[78] Michael Power, *The Risk Management of Everything: Rethinking the Politics of Uncertainty* (Demos 2004); Michael Power, 'The Risk Management of Everything' (2004) 5 Journal of Risk Finance, The 58.
[79] Rothstein, Huber and Gaskell (n 70) 93.
[80] Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).

Responsive Regulation (RRR).[81] RRR is a progression on Ayres and Braithwaite's classic pyramid of regulatory response to non-compliance.[82] The 'twist', if you will, in RRR is that it encourages regulators to take account of the 'firms' own operating and cognitive frameworks (their 'attitudinal settings')', 'the broader institutional environment of the regulatory regime', 'the different logics of regulatory tools and strategies' 'the regime's own performance' and to changes in any of the aforementioned elements.[83] Understanding the regulatee is, of course, good, old-fashioned common sense. In the context of emerging biotechnologies this approach to regulation seems sensible given the emergence of a literature dedicated to discussing the sheer power of the institution of science, and thus a new political discourse altogether.[84]

In this section I have, I hope, provided a quick overview of the main points relevant to the regulatory background of this project (PBR and RBR are discussed further in chapters III and IV respectively). What is important to understand is that the emergence and establishment of new governance is as much due to attractive political rhetoric as it is due to the advantages of the mechanisms themselves. The following two sections are dedicated specifically to explicating my legal approach (1.4) and ethical approach (1.3). I acknowledge that whilst it is straightforward to 'see' a distinct legal approach emerge from within what is essentially a policy discourse, detecting a distinct ethical approach is somewhat elusive – yet no less important. Uncovering and defining a coherent ethical strand is one of the challenges that this project presents. I will attempt to show how the regulatory theories discussed here apply to the field of emerging biotechnologies. In doing so, it will be necessary to return to some elements touched on in the foregoing discussion and explore them at length in greater depth.

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[81] Robert Baldwin and Julia Black, 'Really Responsive Regulation' (2008) 71 The Modern Law Review 59; Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57).
[82] Ian Ayres and John Braithwaite, *Responsive Regulation: Transcending the Deregulation Debate* (Oxford University Press 1992).
[83] Baldwin and Black (n 81) 61.
[84] Jasanoff, *The Fifth Branch* (n 36); Jasanoff, *Designs on Nature* (n 36).

1.3 Ethical Approach: exploring the relationship between ethics and regulation

I hope to demonstrate in this thesis, the merits of incorporating methods of new governance into the regimes that seek to regulate research in emerging biotechnologies. But, where do ethics feature in this particular regulatory discussion? As I have mentioned, ethics (as a branch of philosophy) does not *easily* find its place within strict regulatory discourse.[85] Regulation is, after all, nothing more than a set of mechanisms; a means of achieving a stated, desired end of a particular kind, namely, control or management of a practice. The stated, desired end is likely to be ethically charged (certainly in the field bioethics), but what of the *mechanisms*? I contend that the mechanisms themselves are neutral, however I acknowledge that ethics plays a vital role in designing regulatory systems and the operation of regulatory regimes. Implementing or even considering the use of regulatory mechanisms presupposes the need to regulate, which is a value judgment – in this sense regulatory mechanisms are not entirely 'neutral'.

Many elements of regulation have an ethical dimension. Within any particular regulatory model, the regulators may/may not act 'ethically' in the implementation and enforcement of a regime; the regulatees may/may not act 'ethically' in following the regime; the externalities of a regime may be subject to scrutiny on 'ethical' grounds; the subject matter being regulated may be 'ethically' controversial, and so on. Above all, it may be ethical *not* to regulate at all or equally, it may be ethical to ban a certain practice outright, and impose the strongest sanctions upon practitioners.[86]

However, I am concerned with the potential implementation of very specific, regulatory methods. There is no body of literature on the topic of ethics vis-à-vis specific regulatory mechanisms that I can reference, and with good reason. One could embark on a study of the 'internal' ethics of a particular regulatory regime, but I conjecture such a project would be nonsensical. To query 'do rules have more inherent ethical

[85] I take this opportunity to reiterate that in this paper the term 'regulation' (and all associated terms) refers to a specific academic discipline, with its own set of theories and methodologies, and a highly stylized, technical language. The term 'regulation' should not be interpreted as it would in ordinary parlance (i.e. as a general, non-specific process of control).

[86] It is important to note also the distinction between the conventional meaning of 'ethical' and the more specific definition of 'ethical' within moral philosophy. Thus, one can determine whether an action is ethical or not by measuring compliance against a set of agreed professional or industrial standards. Yet, these standards may have very little bearing on ethical standards within moral philosophy. In this section I refer to 'ethics' in the context of moral philosophy.

credentials than principles, or vice versa?' is absurd. The purpose of a regulatory regime is to achieve certain outcomes, and so long as the outcomes are achieved, without negative externalities and consequences, it matters not whether the mechanism used was 'command and control' or design-based regulation. The question of whether to use rules or principles or market incentives depends entirely on context.[87] This is not to deny the 'meta-ethics' of regulatory theory; some regulatory mechanisms may be more 'libertarian' in quality, others more 'totalitarian'. However it is important to note that these mechanisms can be manipulated or marketed towards political ends. 'Soft law'[88] does not necessarily lend itself to liberal regimes, and conversely 'command and control' does not necessarily translate into an authoritarian regime. Theoretically, it is possible to design a highly liberal framework by means of 'command and control'. Of course, this might not be practical or efficient, which is why choice of regulatory mechanism is important.[89] What follows are some preliminary thoughts on the scope for ethical discussion in my research; these initial thoughts are developed and explored throughout the case studies.

So as to discern the role of ethics and the extent of that role for the purposes of this project, it is necessary to go back several steps and begin by examining the premise that regulation is in fact required. Suppose, for example, there was a breakthrough in the development of artificial wombs, such that ecto-genesis became a real, rather than theoretical, possibility. Without a doubt, in political, academic and media circles questions of how to regulate would immediately arise. For when faced with an issue of this nature we simply assume that there *must* be some rules (using ordinary meaning of the word) – but why should there *necessarily* be rules? Moreover, which rules? And what justifies those rules? Architects of regulatory regimes cannot always answer these questions, and clearly then, regulation is the wrong starting point.

In order to know how to act – whether to ban a particular line of research or therapy; impose some rules of operation, or none at all – we need to uncover the relevant parties' interests, rights and responsibilities and where they might conflict. In other words, we need to ascertain tensions and potential effects (both good and bad) of a course of action. To do all this, we look to ethics. An ethical inquiry will hopefully

[87] See 5.2.1
[88] See 1.4.2 for a full definition of 'soft law'.
[89] See 5.3.1

elucidate any difficulties and help clarify aims. This is the starting point for developing a sensible, workable regulatory framework. The outcomes of an ethical discussion will contribute towards informing the substantive content and direction of a regulatory regime – and therein lines the interface between ethics and regulation. Ethics sets the parameters the limits for the regulatory regime. In this sense, its role is in the 'pre-regulatory' or 'pre-law' stage. Ethics tells us the 'ought', which is then implemented through a variety of regulatory techniques.

It is important to note that a debate on the ethics is unlikely to return a single answer to the question 'what ought we to do, and why?' Different bioethical approaches will return distinct answers and justifications (this, as I will point out later on is politically problematic). It is not appropriate here to discuss exactly which ethical approach is best and why – that is a philosophical debate I do not wish to enter! However, policy makers will have to adopt a particular ethical approach in order for the ensuing regulatory regime to be coherent and defensible.

Of course, ethics is not the only field that will contribute towards the substantive content of a regulatory regime; economics, political science, pre-existing law, sociology, and of course science (this is not an exhaustive list of relevant disciplines), will all feed into it. Regulatory theorists can then construct an appropriate form of regulation to accommodate the demands of these diverse contributions in so far as is judged necessary.

That, at least, is the idea. In practice, regulating biotechnologies poses some ethical peculiarities of its own that make regulation in this field so difficult. A simple comparison will demonstrate this. As mentioned in the previous section, much modern regulatory theory has developed in the context of environmental regulation.[90] This is significant when considering the ethical dimension. Despite recent controversy over the question of climate change, there is little doubt or disagreement that, for example clean air and clean water are desired, universal benefits. In other words, there is general consensus vis-à-vis the main goals of environmental regulation. It follows that having

[90] By this, I mean technical theories of regulation, as opposed to the development of regulatory regimes in areas of social, political and economic life hitherto left alone. One example is the theory of 'smart regulation', which was initially developed by Gunningham and Grabosky (Gunningham, Grabosky and Sinclair (n 27).) to tackle environmental concerns. Regulators have since adopted the 'smart regulation' approach across a number of policy areas (1.2.3).

consensus on the regulatory goals will a) make the starting point for policymakers and regulators much easier, b) hopefully lend credibility to the regime, and c) even if the form is tweaked and changed by successive governments, maintaining the same goals is infinitely less complicated and troublesome than changing both form and substance.

Consensus is a rare thing in the field of emerging biotechnologies. Government can hold any number of informed and open debates and discussions with all stakeholder groups, but achieving ethical consensus on sensitive issues (such as the moral status of an embryo, for example) are likely to remain elusive. Even if, after thorough research and deliberation a policy is adopted and justified in line with what is deemed the best ethical approach, philosophical debate will continue, not only behind the closed doors of philosophy departments, but in political and social spheres, and the media. Given ethical consensus on the end-goal(s) or issues necessary to defining/articulating the end-goal(s) is almost certainly impossible to achieve, I suggest that the *process* itself of developing a regulatory system becomes increasingly important in lending authority to the framework. That is to say, the 'pre-law' or 'pre-regulatory' activity – the ethical inquiry and consultation process – assumes greater import.

The purpose of this project is to analyse some contemporary regulatory approaches and their applicability to the regulation of emerging biotechnologies. What of the 'end-goal'? The analysis that follows presupposes sympathy for encouraging scientific innovation and progress within a correspondingly liberal, responsible, framework. (These are, of course, very general presuppositions. Admittedly, these presuppositions have not been universally approved and accepted, however it is necessary align oneself to *a* perspective in order move forward and analyse the 'fit' between subject matter and mechanism.) All this will rely on a greater degree of dialogue and communicative action between stakeholders, which I submit, can best be achieved through methods of new governance. It is important to reiterate that the objective of this project is *not* to articulate the ethical justification for pursuing a liberal stance on scientific innovation, but demonstrate how a facilitative framework might be accomplished. To use a parallel example, those working in the field of environmental policy and regulation have developed specific theories and practices designed to encourage innovation – so-called ecological modernisation is one such trend.

Finally, it goes without saying that *good* regulatory systems (certainly within this jurisdiction) operate under the Rule of Law, and in accordance with principles of good regulation – transparent, accountable, proportionate, consistent and targeted.[91] Furthermore, a pre-existing body of law and political processes will seek to safeguard justice, and ensure the consideration of issues such as inter- and intra-generational equity. All this will form part of the underlying ethics of a regulatory regime.

As I have mentioned earlier, the focus of this thesis is not ethics. My principle aims are to put forward an argument for new governance as the methodology of choice in the design of regulatory frameworks for emerging biotechnologies, and elucidate the role of law (as it is traditionally understood – see 1.4) within that framework. When I began this research project, I did not anticipate engaging in a substantive ethical inquiry – and, in truth, nor have I. Nonetheless, attempting to decipher the relationship between ethics and technical regulatory choices and processes (a relationship I would currently characterize as 'arms-length') is one of the themes within this project. In fact, as I proceeded with each case study, the importance of investigating and establishing this relationship deepened and emerged as a key strand that has shaped the direction of this research (in particular, Chapter II), and its findings (see 5.2.4).

[91] Better Regulation Task Force, 'Principles of Good Regulation' (n 14).

1.4 Legal Approach: exploring the relationship between law and new governance

Earlier, I emphasized the characterization of new governance as a definite move away from conventional command and control regimes. In some ways this is the best description of the phenomenon; we know what it is not, and we know it when we see it, but a more precise characterization is tricky. Command and control systems capitalize on *legal authority*[92], epitomizing the Austin/Bentham governance model of 'commands backed by sanctions'. Here, the role of law is very clear. But what is the role of law in new governance systems? The articulation of new governance as the antithesis of traditional regulation should not detract from the important fact that new governance regimes must often co-exist with traditional regimes and operate within a pre-existing framework. For example, the framework and jurisprudence of human rights[93] operates across all micro-regimes in the United Kingdom (where there is a relevant claim), regardless of regulatory provenance, subject matter and style; new governance regimes would have to co-operate accordingly. Moreover, the same legal tools that enable traditional regimes can also be adopted by regimes of new governance or integrated into their structure.

In this section I outline, in broad terms, the relationship between law and new governance as perceived to date. This provides a useful starting point from which I can throughout this thesis: a) reflect further on the interaction between the two, b) analyse and form some conclusions on the nature and dynamics of the relationship between law and new governance, and c) critically evaluate the position of law in new governance regimes.

1.4.1 Relationship models between law and new governance

David Trubek and Louise Trubek have identified a number of relationship models between law and new governance.[94] The authors focus on relationships of *co-existence*, that is to say, where conventional legal regulation and new governance mechanisms

[92] More specifically, instruments of legal authority are, for instance, national laws (e.g. in the UK this would mean legislation and the Common law) and European Union law (e.g. Treaties, Directives, Regulations, European Court of Justice decisions). The enforcement of these regulatory standards is through sanctions, ultimately administered through the courts. The various sources of international law (e.g. treaties, custom, general principles, and juridical decisions and writings) are also sources of legal authority, although more complex in nature than time and space permit discussion here.
[93] Convention for the Protection of Human Rights and Fundamental Freedoms (as amended). as incorporated into UK law via the Human Rights Act 1998.
[94] Trubek and Trubek (n 8).

'operat[e] in the same policy domain'.[95] Three types of co-existence are identified. Firstly, a law and new governance might function in a relationship of *complementarity*: 'When each is operating at the same time and contributing to a common objective but the two have not merged…'[96] Secondly, the relationship between the two systems might be characterized as one of *rivalry*. This occurs when new governance mechanisms have been introduced in an area where there is a pre-existing, operating legal regime, to perform the same regulatory functions. In other words, there is a clear choice between systems (although not necessarily for the regulatee!).

Finally, the relationship might be termed as one of *transformation*. To quote Trubek and Trubek,

> '…we use that term [transformation] to describe configurations in which new governance and traditional law are not only complementary, they are also integrated into a single system in which the functioning of each element is necessary for the successful operation of the other'.[97]

This merits further explanation. Trubek and Trubek distinguish four types of transformative relationships. The first is one where law is used to create new governance regimes: law simply creates the new governance regime and then steps back, regulating the regime only on a procedural level. In other words, operating meta-regulation. The second transformative relationship model is where new governance is the primary regulatory regime, however law provides a safety net to ensure protection of rights. The authors explain:

> 'These processes may have been added to areas that were exclusively covered by traditional legal processes and rights-based systems…the rights-based structures are retained as a safety net available to rights-holders, should the new governance processes prove ineffective'.[98]

Thirdly, a two-tier approach might be adopted, where the law sets minimum standards, and new governance regulates actors who exceed those standards. Finally, law could set a general normative framework, mandating new governance with the task of filling in the details and concretizing the regime.

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[95] Ibid 543.
[96] Ibid.
[97] Ibid.
[98] Ibid 549.

Two points must be made here. Firstly, within these models there is much room for variance, both structurally and substantively. The dynamics of the relationship will, to some extent, depend on the regulatory actors' interpretation of their role and position, and their political power, as well as external forces. All this will translate into the resulting regulatory regime. Categorizing regimes of co-existence as complementarity, rivalry, or transformation can be helpful, but the nuances of micro-regimes ought not to be overlooked. Secondly, the specific new governance approaches to be examined in this project (PBR and RBR, in discrete and mixed-model contexts) might not fit within every model of the law/new governance relationship. Nevertheless, the relationship models identified by Trubek and Trubek provide a useful starting point for analysing the relationship between law and new governance. In chapters III and IV I investigate two specific instances of interaction between (hard) law and (international) new governance in the contexts of stem cell research and synthetic biology respectively.

1.4.2 'Hard' and 'soft' law[99]

A slightly different way of describing the difference between traditional methods of regulation and new governance is to draw a distinction between 'hard' and 'soft' law.[100] Within the European Union context the hard/soft law debate has played out over the past few years, and has been well documented.[101] For example, the European Employment Strategy of Open Method of Co-ordination provides a nice soft-law case study, which is used by Trubek and Trubek as a stepping-stone to reflect on hard/soft law debate. The authors, both proponents of soft law, conclude that,

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[99] See chapters III and IV for two prospective examples of the interaction and complementarity between hard and soft law frameworks. See also 5.3.2

[100] Trubek and Trubek (n 9). This paper clearly and comprehensively enumerates the respective advantages and disadvantages of 'hard' and 'soft' law, using the Open Method of Co-ordination as a case study, and how those advantages and disadvantages translate into the hybrid model.

[101] In addition to the works cited herein (section 1.4.2) see: Sabel and Zeitlin (n 9); Rothstein, Huber and Gaskell (n 70); De Burca (n 9); Graínne de Búrca, 'EU Race Discrimination Law: A Hybrid Model?' in Graínne de Búrca and Joanne Scott (eds), *Law and new governance in the EU and the US* (Hart Publishing 2006); Claire Kilpatrick, 'New EU Employment Governance and Constitutionalism' in Graínne de Búrca and Joanne Scott (eds), *Law and new governance in the EU and the US* (Hart Publishing 2006); Joanne Scott and Jane Holder, 'Law and New Environmental Governance in the European Union' in Graínne de Búrca and Joanne Scott (eds), *Law and new governance in the EU and the US* (Hart Publishing 2006); Charles F Sabel and William H Simon, 'Epilogue: Accountability Without Sovereignty' in Graínne de Búrca and Joanne Scott (eds), *Law and new governance in the EU and the US* (Hart Publishing 2006); James S Mosher and David M Trubek, 'Alternative Approaches to Governance in the EU: EU Social Policy and the European Employment Strategy' (2003) 41 JCMS: Journal of Common Market Studies 63; Gregory Shaffer and Mark A Pollack, 'Hard vs. Soft Law: Alternatives, Complements and Antagonists in International Governance' (2010) 94 Minnesota Law Review 706.

> '…we have to get beyond the idea that there must be a choice between hard and soft law. These are not mutually incompatible, and perhaps the most promising ideas are those that would yoke the two together'.[102]

Hybrid systems containing both hard and soft law are not unlike the transformation relationship model. However, the difference in language and classification is interesting. Using the hard/soft law distinction, repositions the idea of law: by definition new governance or soft law has some inherently legal quality (although the term 'soft' could be interpreted pejoratively). The question of whether it *actually* does is open; certainly soft law systems provide a normative framework, but whether this constitutes law is firstly, dependent on the nature of the system in mind, and secondly, determined by one's jurisprudential outlook. Trubek and Trubek acknowledge the difficulties that new governance/soft law poses for legal theory – 'Proponents of hard law have a theory of the nature of law that makes them incapable of grasping the value of soft-law processes'.[103] Implicit in this is the classic positivist model of (hard) law, which values 'binding, uniform and justiciable norms'.[104] New governance or soft law (I use the terms interchangeably) is still a developing approach. Its proponents are faced with two tasks: firstly, to develop a coherent theory of new governance on its own terms, and secondly, to reconcile new governance in broader, jurisprudential terms, as both a discrete and hybrid system. Other commentators in the field have taken up these questions (see 1.4.3).

1.4.3 Contemporary understandings of the relationship between law and new governance[105]

Graínne de Búrca and Neil Walker have contributed a rigorous critique of the current understandings of law and new governance.[106] They argue that current conceptualizations focus on understanding the relationship in causal terms, based on an empirical rather than theoretical grounding. A coherent theoretical perception is important for three reasons: Firstly, empirical conceptions of the relationship 'presupposes operational definitions of law and new governance',[107] when in fact these

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[102] Trubek and Trubek (n 9) 361.
[103] Ibid 363.
[104] Ibid.
[105] See chapter III and chapter IV for two prospective examples of new governance regimes that can complement traditional legal frameworks
[106] Neil Walker and Graínne de Búrca, 'Reconceiving Law and New Governance' (2007) 13 Columbia Journal of European Law 519.
[107] Ibid 2.

concepts are contested. Secondly, a conceptual comprehension of the relationship will deepen comprehension of the causal relationship; the relationship can be understood in terms of form/structure as well as content. Finally, a conceptual framework is necessary in order to evaluate empirical understandings of the law/new governance relationship. De Búrca and Walker emphasize the importance of establishing a common framework of premises and understandings of 'law' and 'new governance' so as to have a sensible conversation vis-à-vis the relationship between the two.

The authors then recapitulate and critique the two main competing conceptual understandings of the relationship – the spatio-temporal framework and the concept-of-law framework[108] – before advancing their own. De Búrca and Walker reconceive the relationship between law and new governance as normative orders of reflexive universalizability. They submit:

> '…what the species of law and NG have most generally in common is membership of the genus normative order. That is to say, each denotes a special rule-based form of practical reasoning – a method of arriving at conclusions as to what to do in the world that relies on the provision and application of general norms...
>
> 'Putting these various common attributes together, we may thing of both law and NG as normative orders operating within a framework of publicly demonstrable and demonstrated *reflexive universalizability*'.[109]

Implicit in the authors' construction of this relationship of reflexive universalizability is the idea that universalizability presupposes reflexivity and vice versa,[110] hence the relationship between law and new governance. However, this relationship is refined thus:

> '…we must see law and NG as each encapsulating a differently and shiftingly [sic.] balanced commitment to two different clusters of social values associated with the respective poses of universalizability and reflexivity, with law continuing to find its equilibrium closer to the universalizability pole and NG striking the balance closer to the reflexivity pole'.[111]

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[108] Ibid 7–13.
[109] Ibid 14.
[110] Ibid 14–6. I have summarized de Búrca and Walker's thesis in very simple terms. Please see 14 – 17 for the full exposition of this theory
[111] Ibid 15.

The tension within this relationship arises because of the respective clusters of practical imperatives that pertain to law and new governance – social regularity and social responsiveness, respectively. 'It is the balance between these clusters of practical imperatives', say de Búrca and Walker, 'which is most clearly at stake in the conceptual debate around law and NG and which in turn informs and gives meaning to the many causal analyses of their relationship which are now pursued'.[112] It is not within my remit to embark on an exploration of the law/new governance relationship in jurisprudential terms in this thesis, however I acknowledge the necessity for further research on this issue. A deeper, jurisprudential understanding of the law/new governance relationship will allow enable a more sophisticated construction and analysis of future regulatory regimes, and a further ground for assessing the regulatory 'fit' vis-à-vis emerging biotechnologies.

In her opus 'The Renew Deal: The Fall of Regulation and the Rise of Governance in Contemporary Legal Thought'[113] Orly Lobel attempts to lay the groundwork for a reconciliation or understanding of new governance *a propos* legal theory. A sweeping history of the evolution of regulation, 'The Renew Deal' sets out to make sense of the numerous and varied mechanisms we term 'new governance' and lay the groundwork for the development of coherent theory of law that accounts for new governance. Although Lobel's work refers specifically to historical developments in America, she also draws on factual and theoretical developments in Europe to explain the new governance movement.

So, what does new governance mean for law and legal institutions? Lobel writes:

> 'The governance stage fundamentally transforms legal control into a dynamic, reflexive, and flexible regime. Its principles promote the internal self-regulatory capacities of other social fields (or subsystems) with which it interacts. Unlike the regulatory model, it is not self-destructive, but self-sustaining'.[114]

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[112] Ibid 16.

[113] Lobel, 'Renew Deal' (n 9).
See also: Bradley C Karkkainen, 'New Governance in Legal Thought and in the World: Some Splitting as Antidote to Overzealous Lumping' (2004) 89 Minn. L. Rev. 471; Orly Lobel, 'Setting the Agenda for New Governance Research' (2004) 89 Minn. L. Rev. 498; Orly Lobel, 'National Regulation in a Global Economy: New Governance Approaches to 21st Century Work Law' in Kenneth G Dau-Schmidt, Seth D Harris and Orly Lobel (eds), *Encycolpedia of Labor and Employment Law and Economics*, vol 2 (Second, Edward Elgar Publishing 2008).

[114] Lobel, 'Renew Deal' (n 9) 285.

Lobel draws heavily on the systems theory and the legal theory of autopoiesis, developed by Niklas Luhmann, and later Gunther Teubner. Thus, she contextualizes new governance as the meeting point of three overarching projects: social democracy, political legitimacy and economic efficiency. I do not propose to explore a systems theory or legal autopoiesis perspective here – exploring at length the construction of an underlying legal theory that accounts for soft law is outside the scope of this thesis – however, it is important to acknowledge Lobel's theoretical bias.[115] Like the aforementioned commentators,[116] Lobel's vision 'reveal[s] how the emerging governance model can enable us to transcend the false duality of centralized regulation and deregulatory devolution'.[117] In other words, she advocates a transformation relationship or hybrid model of new governance.

Returning now to the issue of how and where (if at all) new governance or 'soft law' is explained in terms of legal theory, Joanne Scott and David Trubek point to gap between the real-world practices that have arisen, and that which we call 'new governance', and the alleged failure of legal theory to account for this type of governance:

> '…whereas a traditional conception of law looks for a unitary source of ultimate authority, new governance is predicated upon a dispersal and fragmentation of authority, and rests upon fluid systems of power sharing. Whereas a traditional conception of law posits hierarchies, and places courts at the center of systems of accountability, new governance posits heterarchy, and often looks outside of the courts in seeking to secure real accountability'.[118]

Whereas de Búrca and Walker point to the failure of commentators to conceptualize the law/new governance relationship, Scott and Trubek go further, and place the failure within the actual discipline of jurisprudence as a discourse detached from reality. Quoting Peter Goodrich, they take the view that jurisprudence is nothing more than a 'form of elite ignorance'.[119]

Failing to account for new governance within the pre-existing legal framework is problematic both practically and theoretically. Looking to the European Union context,

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[115] Walker and de Búrca (n 106).
[116] Trubek and Trubek (n 9); Trubek and Trubek (n 8).
[117] Lobel, 'Setting the Agenda for New Governance Research' (n 113) 498.
[118] Scott and Trubek (n 9) 8.
[119] Ibid 9. See also: P Goodrich, 'Law-Induced Anxiety: Legists, Anti-Lawyers and the Boredom of Legality" (2000) 9 Social and Legal Studies 143.

the authors analyse a series of cases where European Court of Justice has been faced with making a decision on the legality of new governance. The Court's response has varied; at different times they have thwarted, ignored, distorted or engaged with the new governance regime, indicating a gap between practical governance and the practice of law. Warning against the 'gap between the models and standards being employed to assess new governance, and the reality of these mechanism and the principles that they reflect'[120] Scott and Trubek pose three challenges: Firstly, through careful study to uncover the internal principles of new governance; secondly, to revise theoretical structures of law and politics to take account to new governance; finally, in light of the foregoing, to refine the vision and mechanisms of new governance. It is hoped that through the case studies undertaken in chapters III and IV, this thesis will contribute to the third and final challenge (albeit in a limited fashion as my focus is specifically on regulating emerging biotechnologies, rather than a more generalized use of new governance).

As will be clear by this stage, I advocate the use of new governance where appropriate. My position is sympathetic towards hybrid systems; theoretically, mixed-models allow regulators to capture the advantages of hard and soft law to create a strong, sustainable, responsive and nuanced regulatory model. Calculating more precisely the nature and composition of hybrid systems in general, theoretical terms is outside the scope of this thesis. What this thesis does offer are two extended examples of potential hybrid systems from within the field of emerging biotechnologies. These analyses, undertaken in the second and third case studies (chapters III and IV), examine the position of law and legal institutions, where relevant, as well as new governance, within the specific proposed hybrid systems. Trubek and Trubek point out that:

> 'Particular attention needs to be given to developing a theory of hybrids. The discussion of hard/soft hybrids is just beginning. We are seeing more and more instances of such hybrids, suggesting this constellation represents an adaptation of legal culture to new circumstances and challenges. Scholars have yet to develop an explanation for this trend, or to craft the robust theories concerning the relative capacities of hard and soft law that is necessary to create a functional theory of hybrids'.[121]

[120] Scott and Trubek (n 9) 18.
[121] Trubek and Trubek (n 9) 364.

I do not intend to develop a 'functional theory of hybrids' in this thesis – that too is outside my remit. However, through the case studies undertaken in chapter III and IV, I hope that this thesis will contribute to: firstly, the on-going discourse concerning new governance and law; and secondly and more specifically, the current discussions on how best to regulate emerging biotechnologies.

The purpose of this lengthy exposition on the relationship between new governance and law is two-fold. Firstly, to provide some background information, which is essential in order to make sense of the ensuing discussions on the respective roles of law and new governance within the architecture of current regulatory frameworks (here, specifically pertaining to stem cell research (chapter III) and synthetic biology (chapter IV)). For, pre-existing legal frameworks (arising from national, regional or international laws) are inescapable; there are established frameworks governing, for example, the treatment of research subjects, the doctor-patient relationship, and the licensing of medical therapies. Thus, when designing a new regulatory regime (or part-regime) for any emerging biotechnology these pre-existing frameworks must be taken into account. Secondly, to demonstrate the adaptability of new governance methods; it is possible to intertwine new governance mechanisms with traditional regulatory mechanisms in order to create a sophisticated and nuanced regime. In the field of emerging biotechnologies this is important.

In the field of biotechnology regulators are attempting to manage a variety of actions being carried out by a variety of actors – as I have emphasized already, a single approach may not be appropriate. For example, incentives in the form of competitive research grants might be the best method of encouraging innovation and development, PBR and RBR might be the best methods of regulating parts of the research process, and once the research translates into applicable medical therapies, criminal and civil law frameworks might be the best method of deterring reckless or negligent behaviour by practitioners. A hybrid model of governance acknowledges a rationality and cohesion in the above scenario (as opposed to viewing it as a disparate and therefore unsatisfactory collection of regulations), and encourages regulators to recognize related regulatory frameworks. Furthermore, regulatory mechanisms may have different levels of legal authority or status, and this can be effective. I shall explore and address these issues at length in the context of specific case studies that follow.

1.5 Introducing the case studies

The body of this thesis comprises three contrasting case studies in approaches to regulation within the field of emerging biotechnologies. The first case study (chapter II), on GMO regulation in Europe and internationally, demonstrates a regulatory approach that does not operate optimally in the field of emerging biotechnology, namely, traditional command and control. Using the story of a product named 'golden rice', I critique the regulatory regime for failing to provide adequate space for ethical reflection, and the limited role of ethics within the regime. I then suggest an alternative approach. This alternative approach recognizes the multiple contexts in which regulation operates, and offers a multi-layered, multi-track system that is able to accommodate the socio-ethical nuances of the GMO products being assessed.

This first case study is essential in exemplifying many of the regulatory characteristics that I deem undesirable[122] in the context of regulating biotechnologies: inflexibility, lack of reflexivity, lack of nuance within the regime, absence of ethical discussion, absence of participation from all interested/affected parties. The second and third case studies seek to address these 'regulatory undesirables' by offering regulatory solutions, namely through new governance mechanisms, that promote and develop desirable characteristics: flexibility, reflexivity, nuance, ethical forums, regulatory enrolment and participation, and so on.[123]

The second case study (chapter III) focuses on regulating the international dimension of stem cell research. I advocate adopting a polycentric PBR approach through embracing the reach and expertise of the growing network of international organizations concerned with the governance of international stem cell research. I argue that the dynamism PBR brings to the regulatory process, together with its qualitative advantages (adaptability, reflexivity, inter-party dialogue and relationship building) are particularly apposite in the context of international stem cell research.[124] Furthermore, I argue that in many respects such a regime is already in the process of organic development. Parallel to the trend towards cross-jurisdictional scientific collaborations, there are growing number of guidelines and consensus statements issued by non-governmental international

[122] As opposed to 'regulatory desirables': see chapter V (5.2) and: Anne-Maree Farrell and others, 'Regulatory "Desirables" for New Health Technologies' (2013) 21 Medical law review 1.
[123] See section 1.2.1
[124] See section 1.2.4

organizations concerned with the operation of stem cell research globally. I argue that these documents - regulatory collaborations - can be exploited as potential 'soft law' instruments and consider them as the starting point for an international regulatory regime.

The third case study (chapter IV) focuses on the regulation of international commercial gene synthesis. In chapter 4 I advocate adopting a RBR approach,[125] again, by embracing the reach and expertise two international industry groups, namely, the International Association Synthetic Biology and the International Gene Synthesis Consortium. Concerned with the biosecurity risks that synthetic biology poses, these organisations have developed protocols that have been adopted by commercial gene synthesis companies around the world (gene synthesis companies produce material that is used in synthetic biology research, in particular DNA design). Given the issue of 'risk' is a central concern within synthetic biology I argue that RBR offers a pragmatic and appropriate regulatory solution. RBR allows the regulator to target and manage salient risks, across a highly accessible, growing field that is populated by both traceable (formal/academic researchers) and non-traceable (DIY synthetic biologists) participants. Moreover, RBR is adaptable and requires a degree of reflexivity that enables the regime to keep up-to-date with advances in both the technology and our understanding of it. Finally, I demonstrate that the industry protocols are in fact well-aligned with the basic elements of RBR, making them the ideal starting point for establishing a wider-reaching, recognized international regime for commercial gene synthesis.

In chapter V I compare and contrast these three case studies; the first examines a more traditional regulatory approach, whilst the second and third showcase the possibilities available through new governance. Through engaging in a comparative analysis I draw out the characteristics and qualities that, I argue, are conducive to the development of truly facilitative international governance frameworks for emerging biotechnologies.

Finally, a note on the structure and style of this thesis: in accordance with the guidelines of the Doctoral Programme in Bioethics and Medical Jurisprudence each of the following case studies (chapters II, III and IV) are written as stand-alone pieces that may be read independently, as well as part of this thesis as a whole.

[125] See section 1.2.5

CHAPTER II

Considering the role of ethics in regulation: a case study on European and international GMO regulations.

'Eradicating extreme poverty continues to be one of the main challenges of our time, and is a major concern of the international community. Ending this scourge will require the combined efforts of all, governments, civil society organizations and the private sector, in the context of a stronger and more effective global partnership for development.'[126]

- Ban Ki-Moon, UN Secretary-General

2.1 Introduction

The most recent World Food Program study estimates that 925 million people suffer from undernourishment.[127] Of the 925 million, 98% live in the developing world.[128] Improving global health through alleviating poverty and hunger, fighting disease and malnutrition, continue to be at the forefront of governmental, non-governmental and private enterprise agendas. In fact, as can be seen from the quote above, developing programmes to combat ill health is encouraged. Like clean air and clean water, health (at least some measure of it) is an uncontroversial, universal 'good'.[129] By extension, 'good health' as a purpose or goal behind a particular enterprise is *prima facie* ethically uncontroversial.

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126 'We Can End Poverty: Millennium Development Goals and Beyond 2015' (*United Nations Millennium Development Goals*) <http://www.un.org/millenniumgoals/bkgd.shtml> accessed 27 March 2015. Quote continues:
The Millennium Development Goals set time bound targets, by which progress in reducing income poverty, hunger, disease, lack of adequate shelter and exclusion — while promoting gender equality, health, education and environmental sustainability — can be measured. They also embody basic human rights — the rights of each person on the planet to health, education, shelter and security. The Goals are ambitious but feasible and, together with the comprehensive United Nations development agenda, set the course for the world's efforts to alleviate extreme poverty by 2015.

127 Food and Agriculture Organization of the United Nations, 'Global Hunger Declining, but Still Unacceptably High' (2010) <http://www.fao.org/docrep/012/al390e/al390e00.pdf> accessed 27 March 2015.

128 Ibid.

129 Defining 'health' or 'good health' precisely remains outside the scope of this chapter. Notably, the World Health Organisation defines health thus: 'Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity' (Preamble to the Constitution of the World Health Organisation as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organisation, no. 2, p. 100) and entered into force on 7 April 1948). Yet, this definition has come under considerable critique (see for example: M Huber and others, 'How Should We Define Health?' (2011) 343 BMJ d4163.). For a recent discussion on the conceptualization of health see: J Coggon, *What Makes Health Public?: A Critical Evaluation of Moral, Legal, and Political Claims in Public Health*, vol 15 (Cambridge University Press 2012) 11–23.

Today, through genetic modification, it is possible to create stronger crop varieties and (edible) plants enriched with essential micronutrients, which would arguably go some way towards addressing poverty and ill health. However, the production and consumption of genetically modified organisms (GMOs) is a deeply controversial issue. (Of course, all living organisms are genetically modified to some extent through evolution, mutation and reproductive choice; here I am only concerned with laboratory-based genetic modification.) In Europe concerns over potential risks posed by GMOs has resulted in a regulatory regime based upon precaution.[130] However this regime has been accused of disrupting and delaying schemes that could help alleviate malnutrition and disease, and prevent death: the inventors of golden rice, a genetically engineered vitamin-A enriched rice, blame over-zealous regulations for delaying golden rice being brought to market.[131] Regulating biotechnologies is a difficult task as often the technology or procedure is contested on ethical grounds: assisted reproductive technologies, stem cell research, xenotransplantation, human enhancement technologies, and genetic engineering are examples of biotechnologies that have been the subject of ethical debate by media and governments across the world in recent years.[132]

In this chapter I examine the interplay between the socio-ethical issues that biotechnologies present, and the regulation of such technologies, using the continuing story of golden rice as a narrative device through which to enter a discourse on regulation. Focussing on the regulation of GMOs in Europe, I intend to demonstrate i) the necessity for formal space within the regulatory regime for ethical discussion, ii) the role of ethics in the decision-making process, and iii) the failure of the EU to accommodate either of the foregoing. Finally, I offer an alternative regulatory approach based on two concepts: 'regulatory differentiation' and 'streamlining regulation'.

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[130] See 2.2

[131] Ingo Potrykus, 'Regulation Must Be Revolutionized' (2010) 466 Nature 561; Ingo Potrykus, 'Lessons from the "Humanitarian Golden Rice" Project: Regulation Prevents Development of Public Good Genetically Engineered Crop Products' (2010) 27 New Biotechnology 466; Ingo Potrykus, 'Golden Rice and Beyond' (2001) 125 Plant Physiology 1157.

[132] Of course not all biotechnologies provoke virulent social and academic responses; nanotechnology is one such example.

2.1.1 The story of Golden Rice

According to the World Health Organization vitamin-A deficiency is most harmful to children and pregnant women.[133] It is the leading cause of blindness in children: an estimated 250 million preschool children are vitamin A-deficient.[134] Approximately 250 000-500 000 children suffering from vitamin A-deficiency become blind every year, and half die within a year of losing their sight.[135] Furthermore, this deficiency increases the risk of disease and death from common childhood illnesses such as diarrhoea and measles.[136] In pregnant women, a vitamin A-deficiency can cause night blindness and increase the risk of maternal mortality.[137]

In 1999 Ingo Potrykus and his colleagues made a breakthrough in their laboratories: they discovered that 'it was possible to reconstitute the carotenoid pathway in rice grains, something even many experts did not believe was possible'.[138] By doing so, they could create rice grains that produce and accumulate β-carotene, which the body then converts to pro-vitamin A. To briefly and simply explain the science: rice plants contain β-carotene in the green, outer tissues of plant for the purposes of photosynthesis, but not in the endosperm, the starch-storing tissue that is edible. By adding two transgenes, phytoene synthase (*psy*) and phytoene desaturase (*crt* I), Potrykus and his colleagues reconstituted the biosynthetic pathway or added the two 'missing steps' to allowing β-carotene to accumulate in the endosperm.[139] In short, using genetic engineering, Potrykus and his colleagues developed a vitamin-A enriched rice variety. These rice grains appear 'golden' in colour reflecting the concentration of pro-vitamin A; the deeper the colour, the richer the rice is in pro-vitamin A.[140] It is the prevalence of β-carotene that gives carrots, papaya and squash their sunset hue. The breakthrough in 1999 was a valuable proof-of-concept. Since then golden rice has been improved in order to increase the concentration of pro-vitamin A.[141]

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133 'Nutrition - Micronutrient Deficiencies - Vitamin A Deficiency' (*World Health Organization*) <http://www.who.int/nutrition/topics/vad/en/> accessed 27 March 2015.
134 Ibid.
135 Ibid.
136 Ibid.
137 Ibid.
138 'History of the Golden Rice Project' (*Golden Rice Project: Golden Rice Humanitarian Board*) <http://www.goldenrice.org/Content1-Who/who2_history.php> accessed 27 March 2015.
139 'The Science of Golden Rice' (*Golden Rice Project: Golden Rice Humanitarian Board*) <http://www.goldenrice.org/Content2-How/how1_sci.php> accessed 27 March 2015.
140 Ibid.
141 Ibid.

The inventors of golden rice describe their product as part of the solution to the public health problem of vitamin-A deficiency in rice-dependent communities.[142] Golden rice would appear to be a welcome response to widespread vitamin A-deficiency that particularly affects Africa and South-East Asia.[143] Rice is the staple food for many of these communities, particularly those in South-East Asia, therefore golden rice appears to be a simple and sustainable solution. However, golden rice has not yet reached consumers.[144] In an impassioned article written in 2010, Potrykus blamed excessive, unjustified and impractical legalities for the tardiness of this crop reaching farmers and consumers – and ultimately causing illness and death: 'I therefore hold the regulation of genetic engineering responsible for the death and blindness of thousands of children and young mothers'.[145]

Golden rice has hit the UK headlines more recently. In August 2013 a trial crop in the Philippines was destroyed only weeks before it was to undergo safety evaluations.[146] Further interest in the news story developed following the UK Secretary of State for Environment, Food and Rural Affairs, Owen Paterson's statement that those who oppose golden rice are 'wicked'.[147] Asked to comment on the Environment Secretary's statement, Potrykus said, 'He is right. If I understand the meaning of the English word

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142 For example: 'The aim of biofortification is to improve the primary food source of hundreds of millions of people by increasing the nutritional quality of staple crops.' 'Why Golden Rice, Is There a Need for It?' (*Golden Rice Project: Golden Rice Humanitarian Board*) <http://www.goldenrice.org/Content3-Why/why.php> accessed 27 March 2015.
See also: Jorge E Mayer, Peter Beyer and Ingo Potrykus, 'The Golden Rice Project' [2006] Golden Rice Project: Golden Rice Humanitarian Board <http://www.goldenrice.org/PDFs/The_Golden_Rice_Project_Mayer_et_al_2006.pdf> accessed 27 March 2015; Potrykus, 'Regulation Must Be Revolutionized' (n 131).

143 World Health Organisation, 'Global Prevalence of Vitamin A Deficiency in Populations at Risk 1995–2005: WHO Global Database on Vitamin A Deficiency' (2009) <http://whqlibdoc.who.int/publications/2009/9789241598019_eng.pdf?ua=1> accessed 1 April 2015.

144 Golden Rice is currently undergoing field tests. (Telephone interview with Ingo Potrykus, Professor Emeritus, Institute of Plant Sciences, Swiss Federal Institute of Technology, ETH Centre, Chairman Golden Rice Humanitarian Board & Network (Switzerland/Manchester, UK, 6 April 2012))

145 Potrykus, 'Regulation Must Be Revolutionized' (n 131).

146 Matt McGrath, '"Golden Rice" GM Trial Vandalised' (*BBC News - Science & Environment*, 9 August 2013) <http://www.bbc.co.uk/news/science-environment-23632042> accessed 1 April 2015.

147 'GM "Golden Rice" Opponents Wicked, Says Minister Owen Paterson' (*BBC News - UK Politics*, 14 October 2013) <http://www.bbc.co.uk/news/uk-politics-24515938> accessed 1 April 2015; Claire Carter, 'GM Opponents Could "Leave Children to Go Blind"' *Telegraph.co.uk* (14 October 2013) <http://www.telegraph.co.uk/earth/agriculture/geneticmodification/10378652/GM-opponents-could-leave-children-to-go-blind.html> accessed 1 April 2015; Peter Dominiczak and Christopher Hope, 'Children Are Dying because of Failure to Use GM Crops, Says Owen Paterson' *Telegraph.co.uk* (20 June 2013) <http://www.telegraph.co.uk/earth/environment/10131606/Children-are-dying-because-of-failure-to-use-GM-crops-says-Owen-Paterson.html> accessed 1 April 2015.

'wicked' right, I think he is right.'[148] This comes amid a resurgence of political interest in the broader GM debate. A long-time supporter of GM products Paterson has frequently cited golden rice as a positive example of what the technology can achieve.[149] He is a key figure in the current UK government's push to develop and encourage investment in the British GM sector,[150] alongside Prime Minister, David Cameron.[151] In a lengthy and detailed speech at Rothamsted Research[152] in June 2013 that attracted considerable media attention[153] the Environment Secretary argued that 'GM is a safe, proven and beneficial innovation',[154] specifically citing golden rice as an example of the health/nutrition benefits attainable through GM. Importantly, Paterson has called for a fresh debate on GMO's and reconsideration of the regulatory conditions for these technologies in Europe.[155] This chapter then, is a serendipitously timed contribution to the revived discourse on the regulation of GMOs in Europe.

2.1.2 Purpose & remit

Golden rice has attracted as much criticism as it has praise. I do not intend to investigate the utility of golden rice vis-à-vis other means of eradicating vitamin A-deficiency; I advance from the premise that the evidence indicates that this product will be helpful, not harmful, and that some help is better than no help. Nor do I assess the pros and cons of genetic engineering *per se,* for two reasons: Firstly, there is a wide body of literature documenting this debate that need not be repeated.[156] Secondly, GM

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148 BBC Radio 4, 'Genetics and Education; Golden Rice Inventor; Chimp Chatter and Lightning Lab', *Inside Science* (17 October 2013).

149 'Owen Paterson Backs UK-Grown Genetically Modified Food' (*BBC News - UK Politics*, 10 December 2012) <http://www.bbc.co.uk/news/uk-politics-20664016> accessed 1 April 2015; 'GM "Golden Rice" Opponents Wicked, Says Minister Owen Paterson' (n 147); Christopher Hope, 'More GM Crops Means More Nature Reserves, Says Owen Paterson' *Telegraph.co.uk* (20 June 2013) <http://www.telegraph.co.uk/earth/environment/10130995/More-GM-crops-means-more-nature-reserves-says-Owen-Paterson.html> accessed 1 April 2015.

150 Matt McGrath, 'Government Leads New GM Crops Push' (*BBC News - Science & Environment*, 20 June 2013) <http://www.bbc.co.uk/news/science-environment-22967571> accessed 1 April 2015.

151 Hope (n 149).

152 'Rt Hon Owen Paterson MP Speech to Rothamsted Research' (*GOV.UK - Speeches*, 20 June 2013) <https://www.gov.uk/government/speeches/rt-hon-owen-paterson-mp-speech-to-rothamsted-research> accessed 27 March 2015.

153 See for example: Jim Pickard and Clive Cookson, 'UK Government Makes Strongest Statement yet in Favour of GM Food' *Financial Times* (20 June 2013) <http://www.ft.com/cms/s/0f6e7492-d8f5-11e2-84fa-00144feab7de,Authorised=false.html?_i_location=http%3A%2F%2Fwww.ft.com%2Fcms%2Fs%2F0%2F0f6e7492-d8f5-11e2-84fa-00144feab7de.html%3Fsiteedition%3Duk&siteedition=uk&_i_referer=> accessed 1 April 2015. (NB: article behind a pay wall.)

154 'Rt Hon Owen Paterson MP Speech to Rothamsted Research' (n 152).

155 'GM "Golden Rice" Opponents Wicked, Says Minister Owen Paterson' (n 147).

156 Useful summaries of the arguments for and against GMOs can be found at: 'Weighing the GMO Arguments: For' (*Food and Agriculture Organization of the United Nations*) <http://www.fao.org/english/newsroom/focus/2003/gmo7.htm> accessed 27 March 2015; 'Weighing

technology is already in use, therefore to pursue the issue of whether this technology is good or bad, and whether we should use it or not, seems if not futile, at least of low priority. The more pertinent question is the *extent* to which this technology should be used. The purpose of this chapter is to explore the tension between regulation and the ethical claims that underlie regulatees' activities – the story of golden rice provides a good example of this type of conflict. The regulations that apply to golden rice apply equally to any new genetically modified food product wishing to enter the market. Should it matter that golden rice might help prevent blindness, illness and death, whereas other genetically modified products might not have claim to such noble ends, or might simply be luxury or even frivolous products? Regulatory standards apply indiscriminately to all products of a particular class. But are regulations which slow-down humanitarian projects such as golden rice examples of unethical or poor regulation because of this? Or can those regulations be justified? If so, on what grounds? Policymakers are faced with the unenviable task of balancing evidence and reaching a decision; how much weight should ethical claims, such as the *potential* to provide humanitarian aid, be accorded vis-à-vis economic, political, and social considerations, as well as the imperative to design a 'good'[157] regulatory system?

I begin by setting the scene. In sections 2.2 and 2.3 I briefly review the regulations that govern the production and dispersion of genetically engineered products; although the jurisdictional focus is the EU, I refer to international obligations where relevant. I then turn to identify and address some of the tensions and issues that arise from these frameworks: I examine the experience of the European precautionary approach to GMOs and the impact of this approach beyond the boundaries of the EU, as well as critically analysing the structure of the European framework in itself (section 2.4). It is important to note that the purpose of this chapter is not to contribute a critique of the precautionary principle. Yet some critical engagement with the continuing 'pro-actionary'/precautionary debate[158] is necessary to fully appreciate the European regime

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the GMO Arguments: Against' (*Food and Agriculture Organization of the United Nations*) <http://www.fao.org/english/newsroom/focus/2003/gmo8.htm> accessed 27 March 2015; Food and Agriculture Organization of the United Nations, 'Genetically Modified Organisms, Consumers, Food Safety and the Environment' (2001) FAO Ethics Series 2 <http://www.fao.org/3/a-x9602e.pdf> accessed 1 April 2015.

157 Better Regulation Task Force, 'Principles of Good Regulation' (n 14).

158 Andy Stirling, 'Why the Precautionary Principle Matters' (*The Guardian: Political Science blog*, 8 July 2013) <http://www.theguardian.com/science/political-science/2013/jul/08/precautionary-principle-science-policy> accessed 1 April 2015; Steve Fuller, 'Beyond the Precautionary Principle' (*The Guardian: Political Science blog*, 10 July 2013) <http://www.theguardian.com/science/political-science/2013/jul/10/beyond-

and set the context for the alternative approach proposed in section 2.5. Throughout this chapter, my focus is on the interaction between regulation and ethical claims pertaining to GMOs.

precautionary-principle> accessed 1 April 2015; Tracey Brown, 'The Precautionary Principle Is a Blunt Instrument' (*The Guardian: Political Science blog*, 9 July 2013) <http://www.theguardian.com/science/political-science/2013/jul/09/precautionary-principle-blunt-instrument> accessed 1 April 2015; Jack Stilgoe, 'You're Sure of a Big Surprise' (*The Guardian: Political Science blog*, 10 July 2013) <http://www.theguardian.com/science/political-science/2013/jul/10/science-policy1> accessed 1 April 2015; Alice Bell, 'What's All the Fuss about the Precautionary Principle?' (*The Guardian: Political Science blog*, 12 July 2013) <http://www.theguardian.com/science/political-science/2013/jul/12/precautionary-principle-science-policy> accessed 1 April 2015.

2.2 The Precautionary principle/approach

In order to appreciate both the European and international regulatory frameworks, it is necessary to provide a brief exposition of the precautionary principle/approach.[159] Some of the key tensions and issues pertaining to the adoption of this particular regulatory approach are discussed in following section (2.3) and in section 2.4.

The Precautionary Principle has origins in environmental policy, and was most famously articulated in the Rio Declaration on Environment and Development:

> 'Principle 15. 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.'[160]

Other notable formulations of the principle may be found in the Wingspread Consensus Statement on the Precautionary Principle (1998), [161] European Commission Communication on the Precautionary Principle (2000),[162] and the Cartagena Protocol on Biosafety (2000).[163] A simple, useful articulation of the precautionary principle within the context of European jurisprudence states that:

> '…where there is uncertainty as to the existence or extent of risks to human health [or animal health or the environment] protective measures may be taken without having to wait until the reality and seriousness of those risks become fully apparent.'[164]

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159 I use the terms 'precautionary principle' and 'precautionary approach' interchangeably.

160 UNEP, Rio Declaration on Environment and Development (adopted 3-14 June 1992), United Nations Conference on Environment and Development (Rio de Janeiro, Brazil). UN Doc. A/CONF.151/26 (vol. I) / 31 ILM 874 (1992) (hereafter 'Rio Declaration')

161 'Wingspread Conference on the Precautionary Principle: The Wingspread Consensus Statement on the Precautionary Principle' (*Science & Environmental Health Network*, 26 January 1998) <http://www.sehn.org/wing.html> accessed 27 March 2015.

162 European Commission, 'Communication from the Commission on the Precautionary Principle' COM (2000) 1 final

163 Secretariat of the Convention on Biological Diversity (2002), Cartagena Protocol on Biosafety to the Convention on Biological Diversity: text and annexes (adopted 29 January 2000, entered into force 11 September 2003) Montreal, Canada (henceforth 'Cartagena Protocol')

164 Case C-157/96 *National Farmers' Union* [1998] ECR I-2211 and Case C-180/96 *United Kingdom v. Commission* [1998] ECR I-2265.

Please note that this is just one example of the formulation of the precautionary principle. The principle can be traced through the jurisprudence of the European Court of Justice, as well as legislative documents such as the Treaty on the European Union (Consolidated versions of the Treaty on European Union and the Treaty on the Functioning of the European Union 2012/C OJ 326/01). For an analysis of the application of the principle in within the EU see: Elizabeth Fisher, *Risk Regulation and Administrative*

The precautionary principle is subject to interpretation and characterized as narrow/wide, weak/strong and so forth. As Farrell writes, 'How it is applied seems to vary at times between policy sectors, as well as between different political and legal orders, thus making any claim to universality in approach a tenuous one'.[165] However, at the core is the issue of managing scientific uncertainty.[166] This has led to a number of criticisms. Firstly, the changeable character of the principle has meant that clarity, consistency, and certainty[167] remain elusive, leading some to characterize it as a 'state of mind' rather than a formal risk governance process.[168] Secondly, it has been accused of providing an excuse for state-protectionism.[169] Sunstein has pointed out the propensity of this principle to exacerbate the fear-factor, leading to decisions based on emotion rather than scientific evidence.[170] Finally, the principle has been charged with stifling the decision-making process by requiring an answer to the risk assessment one-way or the other at the expense of the middle ground.[171] In response to these criticisms, proponents of the principle claim that science is incorporated not marginalized, into the mechanism of the principle, and that it is important to acknowledge the limits of science.[172] But, as Farrell points out,

> 'Calling for its application in this context simply acknowledges that there may be a need for political leadership and responsibility for taking action in the face of sciences' limitations in quantifying risk. How best to reconcile the relationship between science and politics in applying the precautionary principle is the issue that lies at the heart of much of the controversy over its use…
>
> What has been recognized, however, is that the failure to define more clearly the parameters of the science-politics relationship in relation to the use of the

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Constitutionalism (Reprint, Hart Publishing 2010); Nicolas de Sadeleer, 'The Precautionary Principle in EC Health and Environmental Law' (2006) 12 European Law Journal 139; Joseph Corkin, 'Science, Legitimacy and the Law: Regulating Risk Regulation Judiciously in the European Community' (2008) 33 European Law Review 359.

165 Anne-Maree Farrell, *The Politics of Blood: Ethics, Innovation and the Regulation of Risk* (1st edn, Cambridge University Press 2012) 169. See also: Giandomenico Majone, 'What Price Safety? The Precautionary Principle and Its Policy Implications' [2002] Journal of Common Market Studies 89.

166 Farrell (n 165) 166–197; Pat O'Malley, *Risk, Uncertainty and Government* (Routledge 2012).

167 Bearing in mind that these are key elements of 'good regulation', as characterized by the 'Better Regulation' movement. See: Better Regulation Task Force, 'Principles of Good Regulation' (n 14).

168 Silvio Funtowicz and others, 'Science and Governance in the European Union: A Contribution to the Debate' (2000) 27 Science and Public Policy 327.

169 Ibid.

170 CR Sunstein, *Laws of Fear: Beyond the Precautionary Principle*, vol 6 (Cambridge University Press 2005).

171 Ibid.

172 J Steele, *Risks and Legal Theory* (Hart Publishing 2004).

> precautionary principle may result in prolonged periods of indecision, as well as the stifling of innovation.'[173]

Deciding whether or not to regulate an activity and if so, how to regulate the activity (i.e. the regulatory approach and tools selected) is a political decision; the precautionary principle is one tool at regulators' disposal. But the tricky relationship between science and politics in this context prompts the question of whether the precautionary principle is being exploited as a political tool, that depending on its articulation and application, incorporates to some extent, a scientific risk assessment? If so, the principle is open to attack on yet another ground. When is it appropriate to apply the principle? And what is the burden of proof – a balance of probabilities or beyond reasonable doubt or something else entirely? Furthermore, the merits or demerits of this principle would appear to be dependent on what exactly what one chooses to apply precaution to. In the context of GMOs, in so far as a product such as golden rice is concerned, one might argue that the principle is oddly weighted: in favour of an uncertain harm (damage to environment, human and/or animal health) and against a certain harm (poverty, ill health and loss of human life as a result of micro-nutrient deficiency). If it is for the proponents of genetic engineering to discharge the burden of proof, what more is required? It would appear that in order to benefit from the protections bestowed by the precautionary principle, the activity in question must be politically attractive.

I will return to some of these issues later. For the present, it is sufficient to bear in mind the precautionary principle and the tensions pertaining thereto, whilst exploring the regulatory frameworks relevant to GMOs.

[173] Farrell (n 165) 169–70.

2.3 An overview of the global GMO regulatory framework

2.3.1 European Union regulations

Within the European Union a matrix of Directives and Regulations govern the production and supply of GMOs.

Directive 2001/18/EC[174] governs the deliberate release of GMOs into the environment for a) experimental purposes, and b) placing a GMO product (the definition of which includes a product containing GM material) on the market, in accordance with the precautionary principle. This is reiterated throughout, and clearly enshrined in Article 4:

> 1. Member States shall, in accordance with the precautionary principle, ensure that all appropriate measures are taken to avoid adverse effects on human health and the environment which might arise from the deliberate release or the placing on the market of GMOs…[175]

The Directive details the standards and procedures, including the risk assessment methodology, required in order obtain approval for a GMO product to be released within the EU, as well as the post-release monitoring and control obligations. The approval process is lengthy, cumbersome and involves many steps.[176] Consent for release of a GMO product is granted for a 10-year period, and may be renewed.[177] Directive 2001/18/EC retains the controversial so-called 'safeguard clause' from Directive 90/220/EEC. Strictly speaking, authorisation of a GMO implies free movement throughout the internal market; however Article 23[178] gives Member States the right to provisionally restrict or prohibit the use and/or sale of an approved GMO product within its territory.

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[174] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC (henceforth 'Directive 2001/18/EC')
Directive 2001/18/EC repealed Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms [1990] OJ L 117/15

[175] Directive 2001/18/EC, article 4

[176] 'Press Release - Questions and Answers on the Regulation of GMOs in the European Union' (*European Commission - Press release*, 26 March 2007) <http://europa.eu/rapid/press-release_MEMO-07-117_en.htm> accessed 27 March 2015.

[177] For a list of approved GMO's and renewal status see: 'EU Register of Authorised GMOs' (*European Commission*) <http://ec.europa.eu/food/dyna/gm_register/index_en.cfm> accessed 27 March 2015.

[178] Directive 2001/18/EC, article 23

Directive 2001/18/EC operates in conjunction with Regulation 1829/2003 on GM Food and Feed,[179] which sets out the authorisation procedure specifically for placing on the market GM food or animal feed (intended for consumption by humans or animals). Thus, there are two separate procedures for authorisation in operation, and in some instances the applicant may have a choice as to which authorisation route to follow. The applicant may either submit a single application under Regulation 1829/2003 *but also in compliance with* the provisions for deliberate release into the environment under Directive 2001/18/EC. Or, the applicant may split her application and submit separate applications under the Directive 2001/18/EC and Regulation 1829/2003 respectively. Furthermore, in order to avoid confusion and duplicate applications, an approval under Regulation 1829/2003 authorises the product in question to be marketed as both food and feed. Streamlining these procedures, and allowing businesses to perform a single risk assessment for all uses, is part of the EU's commitment to the 'one door, one key' policy.[180]

The distinction and overlap between the remit of these two instruments is best demonstrated by example.[181] Suppose I own a successful international produce company, whose headquarters are based in Scotland. My Australian subsidiary company has recently developed, through genetic modification, a new variety of apple, which features a subtle vanilla flavour and vibrant cherry-red appearance. I wish to grow this apple variety in my Scottish orchards, and sell them within the internal market. In order to grow my apples in Scotland, I will require authorisation under Directive 2001/18/EC for deliberate release of GMOs into the environment. If I wish to place the apples on the market for food use, I will also require authorisation under Regulation 1829/2003 as my product qualifies as GM food and/or feed under the Regulations. Note that growing GM products and marketing GM products are independent stages, subject to different provisions. If, having considered the climate conditions, I decide not to grow the apples in Scotland, but simply to import them for sale from Australia, I would still require authorisation under the Directive as the apples would have the potential to grow

[179] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed OJ L 268/1 (henceforth 'Regulation 1829/2003')
[180] 'GMOs in a Nutshell' (*European Commission*, 30 April 2009)
<http://ec.europa.eu/food/food/biotechnology/qanda/b2_en.htm> accessed 27 March 2015.
[181] For a pithy summary see: 'The Two Laws Governing Genetically Modified Plants' (*GMO Compass*)
<http://www.gmo-compass.org/eng/regulation/regulatory_process/158.two_laws_governing_genetically_modified_plants.html> accessed 27 March 2015.

somewhere and thus infiltrate the environment within the Directive's jurisdiction. Suppose however, my Australian subsidiary in addition to selling fresh produce, also used the GM fruit to create a line of frozen fruit pies. Instead of importing, growing and selling fresh apples, I decide to only to import and sell the frozen fruit pies, which contain processed GM apple. Under these circumstances, I would only require authorisation under Regulation 1829/2003.

Regulation 1830/2003 on Traceability and Labelling[182] amends and supplements the limited provisions found in Directive 2001/18/EC. It applies to all authorised GMOs (that is to say, all GMOs including products containing or consisting of GMOs) within the EU. These provisions aim to facilitate monitoring and control of GMOs throughout the EU, as well as ensuring consumers retain a degree of freedom of choice. Moreover, 'traceability should also facilitate the implementation of risk management measures in accordance with the precautionary principle.'[183] Traceability requires those who either place or receive a product within the market to keep records (for five years) of their suppliers and those to whom they supply, disclosing in writing the GMO content of the product(s) in question. All pre-packaged products consisting of or containing GMOs must be clearly labelled as such. Non-pre-packaged products, such as products offered to the consumer in a restaurant, must also include this notification on or within vicinity of the product display. GM food and feed authorised under Regulation 1829/2003 are subject to specific labelling requirements as regards the composition of the product, for example, oil or corn gluten feed obtained from transgenic maize must be labelled as such.[184]

Because of the environmental co-existence of GM and conventional (non-GM) products, it is impossible to guarantee a product as 100% GM-free. Therefore at present, products created conventionally, but that may have been accidentally contaminated by GMOs during the production and supply process, may be exempt from the tracing and labelling requirements. If a conventional product, through

[182] Regulation (EC) No 1830/2003 of the European Parliament and of the Council of 22 September 2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC [2003] OJ L 268/24

[183] 'Regulation 1830/2003, section 3

[184] Note however, that under Regulation 1830/2003, milk, eggs or meat obtained from animals fed with GM feed are not subject to traceability or labelling rules.

adventitious or technically unavoidable circumstances, contains traces of authorised GMOs below 0.9%, it is exempt from the traceability and labelling requirements.

In June 2011, in response to political and economic issues arising from asynchronous authorisation, the European Commission adopted Regulation EC 619/2011 that harmonises the zero-tolerance policy on GM feed with an expired or pending authorisation.[185] Prior to Regulation EC 619/2011 there was no central policy on the low-level presence of unauthorised GMOs in feed and Member States adopted individual policies resulting in legal uncertainty for businesses marketing feed imported from outside the EU. The new Regulation sets the acceptable level of GM material in feed at 0.1% (i.e. a technical 'zero') and lays out a system of controls. This Regulation demonstrates the EU's recognition of the need to manage the issue of low-level presence of unauthorised GMOs in imported products – an incident that is likely to increase as more and more countries begin to use genetic engineering in agri-business.

Finally, Regulation 1946/2003 on Transboundary Movement of GMOs[186] systematizes the movement of GMOs between the EU and non-EU countries. Regulation 1946/2003, together with Directive 2001/18/EC, and a number of other instruments, implements the Cartagena Protocol on Biosafety[187] to which the EU is party (see 2.3.2). The Cartagena Protocol establishes an international regulatory framework for the transboundary movement of living modified organisms (a term which is widely used synonymously as GMO), based upon notification, exchange of information, and consent. The Cartagena Protocol, and accordingly Regulation 1946/2003, distinguishes between GMOs for deliberate release into the environment and GMOs intended for food or feed.

The legislative framework in operation throughout Europe is strict; careful risk assessment is required for each GMO, which results in a lengthy, onerous process.[188]

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[185] Commission Regulation (EU) No 619/2011of 24 June 2011 laying down the methods of sampling and analysis for the official control of feed as regards presence of genetically modified material for which an authorisation procedure is pending or the authorisation of which has expired [2011] OJ L166/9

[186] Regulation (EC) No 1946/2003 of the European Parliament and of the Council of 15 July 2003 on transboundary movements of genetically modified organisms [2003] OJ L 287

[187] Cartagena Protocol (n 163)

[188]European Commission, 'Environment Fact Sheet: Genetically Modified Organisms' (2005) <http://www.envirocentre.ie/includes/documents/genitically%20modified%20organisms%20%5B1%5D.pdf> accessed 27 March 2015; J Davison, 'GM Plants: Science, Politics and EC Regulations' (2010) 178 Plant Science 94; D Vogel and D Lynch, 'The Regulation of GMOs in Europe and the United States: A

Despite attracting criticism, and developing acrimonious trade-relationships with more liberal nations,[189] the EU shows little sign of significantly relaxing the provisions. On the contrary, two recent independent reviews of the legislative framework[190] heralded it as 'on the right track'.[191] In a statement to the press John Dalli, Health and Consumer Policy Commissioner, stated that:

> 'These reports confirm that the problems of implementation of the GMO legislation do not stem from its design or its objectives, which remain relevant, but rather from the way these sensitive issues are handled at a political level.'[192]

The principle criticisms and correlating recommendations found in the reports refer to the inefficiency of the authorisation process, the lack of flexibility for GMO cultivation, and need for further harmonisation of risk assessment within the internal market.[193] Importantly, the reports note the socio-political dimension of this regulatory framework as well as economic concerns.

The European GMO legislative framework is grounded in strict science-based assessments; despite this, several Member States invoke what are known as the national

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Case-Study of Contemporary European Regulatory Politics' [2001] New York/Washington: Council on Foreign Relations; R Daniel Kelemen and David Vogel, 'Trading Places: The Role of the United States and the European Union in International Environmental Politics' (2010) 43 Comparative Political Studies 427; Ragnar E Löfstedt and David Vogel, 'The Changing Character of Regulation: A Comparison of Europe and the United States' (2001) 21 Risk Analysis 399; David Vogel, 'Ships Passing in the Night: GMOs and the Contemporary Politics of Risk Regulation in Europe' (European University Institute 2001) RSCAS Working Paper 2001/16 <http://cadmus.eui.eu/bitstream/handle/1814/1725/01_16.pdf?sequence=1> accessed 1 April 2015; David Vogel, 'The Hare and the Tortoise Revisited: The New Politics of Consumer and Environmental Regulation in Europe' (2003) 33 British Journal of Political Science 557; David Vogel, 'The New Politics of Risk Regulation in Europe' [2001] CARR Discussion Papers <http://www.lse.ac.uk/CARR> accessed 19 March 2015; 'Biotechnology: MEPs Vote for the World's Strictest GMO Legislation' (*Europolitics*, 4 July 2002) <http://www.europolitics.info/biotechnology-meps-vote-for-the-world-s-strictest-gmo-legislation-artr189286-10.htm> accessed 29 March 2015; 'Biotechnology, Legislation: MEPs Go for Zero Tolerance on GM Labelling' (*European Research Headlines*, 15 July 2002) <http://ec.europa.eu/research/headlines/07-2002.html#04> accessed 29 March 2015.

[189] See section 2.3.2 'International regulations'

[190] European Commission - Directorate General for Health and Consumers and others, 'Evaluation of the EU Legislative Framework in the Field of GM Food and Feed' (2010) <http://ec.europa.eu/food/food/biotechnology/evaluation/docs/evaluation_gm_report_en.pdf> accessed 1 April 2015; European Policy Evaluation Consortium, GHK Consulting and Technopolis, 'Evaluation of the EU Legislative Framework in the Field of Cultivation of GMOs under Directive 2001/18/EC and Regulation (EC) No 1829/2003, and the Placing on the Market of GMOs as or in Products under Directive 2001/18/EC.' (2011) 30256315 <http://ec.europa.eu/food/food/biotechnology/evaluation/docs/gmo_cultivation_report_en.pdf> accessed 1 April 2015.

[191] 'GMOs: EU's Legislation on the Right Track, Evaluation Reports Conclude' (*European Commission - Press release*, 28 October 2011) <http://europa.eu/rapid/press-release_IP-11-1285_en.htm?locale=EN> accessed 29 March 2015.

[192] Ibid.

[193] European Commission - Directorate General for Health and Consumers and others (n 190); European Policy Evaluation Consortium, GHK Consulting and Technopolis (n 190).

safeguard measures – technically, a scientific justification – as a means of expressing their ethical or social objections to GMOs.[194] In other words, hiding behind a *faux* scientific screen. This lack of 'space' within the framework for ethical and social concerns is an issue I will return to later. For now, it is imperative to note the most recent amendments to Directive 2001/18/EC, as they introduce alternative grounds for Member States to justify banning GMO cultivation.

On 13 July 2010, the European Commission published a proposed amendment[195] with the intended effect of giving Member States the freedom to *restrict or prohibit the cultivation of authorised GMOs* within their territory, without prejudice to the pre-existing grounds for restriction or prohibition, namely serious risk to health and environment.[196]

Accordingly, on 11 March 2015 the Presidents of the European Parliament and Council signed new legislation giving effect to the Commission's proposal.[197] The new Directive 2015/412/EU amends Directive 2001/18/EC by inserting a number of new articles; most notably, Article 26b on 'Cultivation'. Under Article 26b(1) Member States can demand for part or all of their territory to be excluded from the scope of geographical authorization of a GMO either during the authorisation procedure or during the renewal of authorisation procedure. Furthermore, under Article 26b(3) a Member State can restrict or prohibit cultivation of an authorized GMO in all or part of its territory –

> '…provided that such measures are in conformity with Union law, reasoned, proportional and non-discriminatory and, in addition, are based on compelling grounds such as those related to:
>
> (a) environmental policy objectives;

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194 The national safeguard measures are found in Article 16 of Directive 90/220/EEC *as replaced by* Article 23 of Directive 2001/18/EC, which states that:
Where a Member State, as a result of new or additional information made available since the date of the consent and affecting the environmental risk assessment or reassessment of existing information on the basis of new or additional scientific knowledge, has detailed grounds for considering that a GMO as or in a product which has been properly notified and has received written consent under this Directive constitutes a risk to human health or the environment, that Member State may provisionally restrict or prohibit the use and/or sale of that GMO as or in a product on its territory.'
There are at present a number of bans in place under the safeguard clause; see M Sabalza and others, 'EU Legitimizes GM Crop Exclusion Zones' (2011) 29 Nature biotechnology 315.

195 European Commission, 'Proposal for a Regulation of the European Parliament and of the Council amending Directive 2001/18/EC as regards the possibility for the Member States to restrict or prohibit for cultivation of GMOs on their territory', COM (2010) 375 final

196 Directive 2001/18/EC, article 23; Regulation 1829/2003 article 34

197 Directive (EU) 2015/412 of the European Parliament and of the Council of 11 March 2015 amending Directive 2001/18/EC as regards the possibility for the Member States to restrict or prohibit the cultivation of genetically modified organisms (GMOs) in their territory [2015] OJ L 68 (henceforth 'Directive 2015/412/EU)

(b) town and country planning

(c) land use

(d) socioeconomic impacts

(e) avoidance of GMO presence in other products without prejudice to Article 26a

(f) agricultural policy objectives

(g) public policy.

Those grounds may be invoked individually or in combination, with the exception of the ground set out in point (g) which cannot be used individually…'[198]

Directive 2015/412/EU gives Member States a significant amount of freedom to shape their national GMO policy and practice. Two points may be gleaned from this latest episode in the history of European GMO regulation. Firstly, the amendments arguably fuel the restrictive attitude to GMOs that is already prevalent throughout Europe – indeed, the very fact that such amendments have been enacted speaks to this. Secondly, the explicit references to socio-economic and public policy grounds as a recognized reason for restricting/prohibiting GMO cultivation might provide a route into discussing and bringing to the fore the underlying ethical conflicts. However, until the Directive comes into force on 2 April 2015, and is put into practice, it is difficult to comment on the scope and potential impact of this amendment – for instance, how precisely will 'socio-economic' and 'public policy' be interpreted (by Member States, the Commission, and potentially the Courts)?

2.3.2 International regulations

The process of developing and supplying GMOs is subject to a number of international obligations, principally the Cartagena Protocol on Biosafety, [199] the Codex Alimentarius,[200] and WTO jurisprudence.

The Cartagena Protocol on Biosafety, a supplementary agreement to the Convention on Biological Diversity, is an international treaty that came into force in September 2003. The Cartagena Protocol harmonizes the transboundary movement of GMOs and seeks

[198] Directive 2015/412/EU, article 26b(3)

[199] Cartagena Protocol (n 163)

[200] The Codex comprises a number of standards, guidelines, codes of practice and advisory texts that can be found at: 'List of Standards' (*CODEX Alimentarius: International Food Standards*) <http://www.codexalimentarius.org/standards/list-of-standards/> accessed 29 March 2015.

to safeguard biological diversity from risks presented by GMOs in accordance with the precautionary principle. Article 1, which sets out the 'Objective' of the protocol, states:

> 'In accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Protocol is to contribute to ensuring 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, taking also into account risks to human health, and specifically focussing on transboundary movements.'[201]

At the time of writing 168 countries were parties to the treaty,[202] however several major trading nations including the United States of America, Canada and Australia are not party to the treaty, thus limiting its outreach and impact. The main procedures established by the Protocol are the advance informed agreement (set out in Articles 7 – 12, and Annexes I and II) and risk assessment procedures (Article 15, Annex III). In addition, the Protocol establishes a Biosafety Clearing House to facilitate procedural obligations and the international exchange of information (Article 20). Finally, the Protocol imposes upon parties a duty to cooperate with capacity-building (Article 22), and promote public awareness and participation (Article 23).

The Codex Alimentarius Commission, established by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) in the 1960's, is an international food standards agency. The Commission sets food standards, guidelines and codes of practice that 'contribute to the safety, quality and fairness of…international food trade',[203] including guidelines on the use of GM crops. At present the Codex Commission represents 99% of the world population.[204] Although Codex documents are not binding, they are widely used by governments and international agencies as a point of reference and guidance.[205] The World Trade Organisation (WTO) refers to Codex standards vis-à-vis the international trade of GMOs in two agreements: the Sanitary and Phytosanitary Agreement (SPS) and the

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[201] Cartagena Protocol (n 163), article 1

[202] United Arab Emirates was the last country to ratify the protocol on 12 September 2014, at the time of writing (March 2015). 'The Cartagena Protocol on Biosafety' (*Home: The Cartagena Protocol on Biosafety*, 18 March 2015) <http://bch.cbd.int/protocol> accessed 4 April 2015.

[203] 'About Codex' (*CODEX Alimentarius: International Food Standards*) <http://www.codexalimentarius.org/about-codex/en/> accessed 29 March 2015.

[204] Ibid.

[205] This resonates with the type of soft-law governance referred to in chapter I (see particularly 1.2.1, 1.4.2) and explored at length in chapters III and IV.

Technical Barriers to Trade Agreement (TBT). Under the SPS Agreement members of the WTO may temporarily block trade in the interests of protecting public health. The TBT Agreement sets out a requirement that the national regulations of those countries that are members of the WTO do not unnecessarily restrict international trade.

The tension between conservative and liberal policy in relation to GMOs has led to trade disputes between nations. In May 2003 USA, Canada and Argentina[206] filed complaints with the WTO on the following grounds:

(i) Alleged general EC moratorium on approvals of biotech products;
(ii) EC measures allegedly affecting the approval of specific biotech products; and
(iii) EC member State safeguard measures prohibiting the import/marketing of specific biotech products within the territories of these member States.[207]

In September 2006 the Panel circulated their findings (this report was subsequently adopted by the WTO Dispute Settlement Body in November 2006), namely that the EC was in violation of the SPS Agreement on three grounds: firstly, due to the *de facto* moratorium on approving GM products instated by the EC between 1998 and 2004 (a fact that the EC had categorically denied before the Panel), secondly, due to the delays encountered in the authorisation process of GMOs, and finally, that the national safeguard measures were not based on apposite risk assessment.[208] The implementation of this ruling is on-going.

I have provided an overview of the legislative framework from an EU perspective by way of relevant background.[209] The regulations are much more detailed and complex in operation than I have perhaps indicated. However, my intention in this chapter is not to provide an exhaustive review of the legislative framework, but to reflect on a few issues that have arisen from this framework, which I turn to now.

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[206] World Trade Organisation Dispute Settlement, *European Communities – Measures Affecting the Approval and Marketing of Biotech Products* (29 September 2006) WT/DS291/R; WT/DS292/R; WT/DS293/R
[207] Ibid.
[208] Ibid.
[209] In addition to the regulations outlined above, there are national and international intellectual property laws with which to comply. An outline of this body of jurisprudence is outside the scope of this chapter; moreover it is not necessary to the principle argument.

2.4 Assessing the global GMO regulatory framework: issues and discussion

2.4.1 Preliminary points

What I hope will now be clear from the preceding section, is the stern and exacting nature of the GM regulatory framework within the European Union, if not on paper, then certainly in practice. A particular interpretation of the precautionary principle is embedded into the framework in the rule-books and in practice. The precautionary principle is underpinned by a scientific risk assessment, and likewise the plethora of legal instruments that comprise the GMO regulatory framework all insist upon a scientific evidence-base where possible (as already noted above). This significantly contributes to an impression of a wholly rational, reasonable framework free from political influences, value judgments and so forth. Yet as we have seen in section 2, the precautionary principle itself is a political decision to proceed with precaution in circumstances of uncertainty (as opposed to, for example, the risk-based approach employed in the United States[210]). The precautionary principle itself does not indicate the threshold at which preventative action becomes necessary, this can be low or high depending governmental policy. And, it is somewhat paradoxical that when it comes to predicting and evaluating the impact of genetic modification on human and animal health and the environment, science is unable to provide any meaningful answers. My point is two-fold. Firstly, by invoking the precautionary principle vis-à-vis a particular product/activity one is implicitly accepting that the scientific state of knowledge is uncertain – if it were otherwise there would be no need to resort to the precautionary principle. It follows that science is as yet unable to provide clear data on whether GMOs will cause harm, what those harms are, and the extent of the harms – if at all. Thus, relying so heavily on scientific standards is odd. Secondly, the principle itself hinders any opportunity of obtaining scientific evidence. When a new technology or product is developed the accompanying risks *are* unknown, hence the need for extensive tests, trials and so forth. The European articulation of the precautionary principle advocates shutting down the technology (in this case, GMOs) without providing the opportunity to carry out the scientific tests that might provide evidence pointing to harms or lack thereof. Thorough, multiple, controlled trials on the actual effects of

[210] Sheila Jasanoff, 'Between Risk and Precaution – Reassessing the Future of GM Crops' (2000) 3 Journal of Risk Research 277; Vogel and Lynch (n 188); Löfstedt and Vogel (n 188); Vogel, 'Ships Passing in the Night' (n 188); Vogel, 'The New Politics of Risk Regulation in Europe' (n 188); Kelemen and Vogel (n 188); Vogel, 'The Hare and the Tortoise Revisited' (n 188).

GMOs in humans and animals ought to be welcomed, however the framework as it stands does not encourage this.

Ultimately then, decisions within the GM regulatory framework must be based on something other than science despite the lack of designated 'space' for non-scientific concerns within the regime. This is not entirely surprising. We should not expect science to provide answers to questions that require consideration beyond the confines of a laboratory: politics, economics, public opinion, and ethics all have claims within this process. It is particularly noteworthy that despite the precautionary approach being viewed by some as lending itself to a theoretically more 'deliberative process'[211] the actual operation of the European Union regime cannot truly be described as deliberative. Far from being able to 'facilitate in particular deliberation at the science, policy and society interfaces to which risk management is fully connected',[212] the current framework is geared towards a speedy binary response: failing or satisfying the authorisation process. This may be the fault of poor implementation or institutional attitude, but the point remains. The opportunity to consider non-scientific claims is disregarded in favour of a scientific evidence base – or at least the appearance of it. By over-emphasizing scientific evaluation and risk assessment the regulations fail to adequately acknowledge and consider one important element: the potential science and evidence based *benefits* of GMOs. Seen in this light, the internal logic of European precautionary regime begins to fall apart. Here, science and the requirement of evidence-based policies seem to appear on both sides of the argument but not on both sides of the regulatory effect.

2.4.2 An attitude of precaution

Although it was originally introduced into EC jurisprudence in the context of environmental protection, and as a risk management tool[213] the precautionary principle

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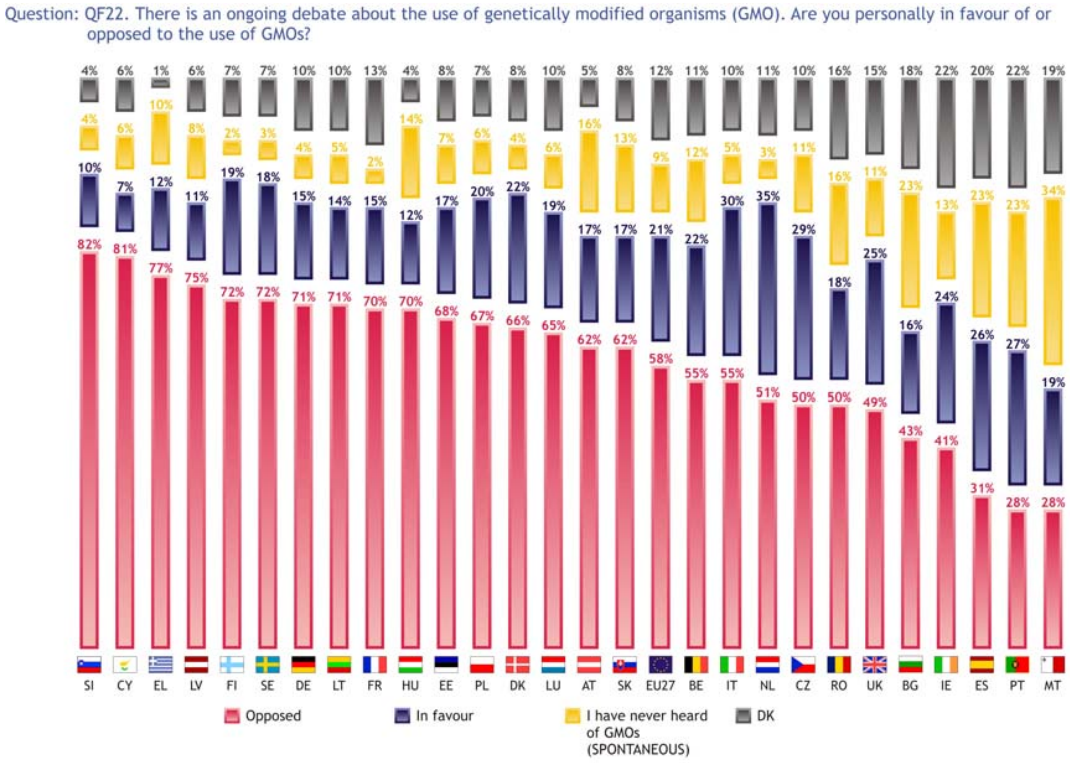
211 Jasanoff, 'Between Risk and Precaution – Reassessing the Future of GM Crops' (n 210); René Von Schomberg, 'The Precautionary Principle and Its Normative Challenges' in Elizabeth Fisher, Judith S Jones and René Von Schomberg (eds), *Implementing the Precautionary Principle: Perspectives And Prospects* (Edward Elgar Publishing 2006). The latter paper draws out different stages of deliberation.

212 Schomberg (n 211) 34; Elizabeth Fisher and Ronnie Harding, 'The Precautionary Principle and Administrative Constitutionalism: The Development of Frameworks for Applying the Precautionary Principle' in Elizabeth Fisher, Judith S Jones and René Von Schomberg (eds), *Implementing the Precautionary Principle: Perspectives And Prospects* (Edward Elgar Publishing 2006).

213 Communication from the Commission on the Precautionary Principle (n 162), paragraph 4 of the Summary reads:

has, I suggest, evolved from a 'principle' of law into an *attitude* ingrained within European juristic and regulatory culture.[214] The extent to which this reflects societal values or vice-versa is tricky to assess. The following table (A) sets out results of a recent EU poll posing the question, 'There is ongoing debate about the use of genetically modified organisms (GMO). Are you personally in favour of or opposed to the use of GMOs?'[215] As can be seen, there is a high level scepticism towards GMO throughout Europe. The report summarises the results thus: 'The majority of Europeans declare that they are opposed to the use of GMOs (58%) while around a fifth (21%) supports their use. A further 9% say they have never heard of GMOs.'[216]

TABLE A: Results of Special Eurobarometer poll to the question: 'There is ongoing debate about the use of genetically modified organisms (GMO). Are you personally in favour of or opposed to the use of GMOs?'[217]



'The precautionary principle should be considered within a structured approach to the analysis of risk which comprises three elements: risk assessment, risk management, risk communication. The precautionary principle is particularly relevant to the management of risk.'

[214] On the evolution of the precautionary principle, the extension of its scope and application see: Sadeleer (n 164).

[215] European Commission - Directorate General Environment; and European Commission - Directorate General Communication, 'Attitudes of European Citizens towards the Environment' (2008) Special EUROBAROMETER 295 65 <http://ec.europa.eu/public_opinion/archives/ebs/ebs_295_en.pdf> accessed 1 April 2015.

[216] Ibid.

[217] Ibid.

A further report comparing polling data between 2005 and 2010 reveals no significant overall change in public perceptions of GMOs throughout Europe, and indicates some decline in support for GMOs.[218]

The GMO trade dispute between America, Canada and Argentina,[219] and the EC forced discussion between the parties, revealing differences in attitude, values, and priorities. As Gareth Davies writes:

> …underlying it [the dispute] is a substantive difference of opinion about GMOs, which at times produced rhetoric suggesting the parties were poles apart. In fact, both parties reluctantly shared two premises. One is that bad things might happen as a result of genetic modification…On the other hand, it is also true that in general, and in the cases under consideration, these things have not happened, even though some of the products have been around for quite a while.[220]

It is the differing reactions and evaluations towards the two agreed upon statements of uncertainty that is interesting. Davies continues:

> The important disagreement was about attitude. Here the Europeans emphasized, in light of the first premise, the need to be precautionary, while the Americans emphasized, using the second, the need not to block progress. It is argued below that the value choices underlying this difference are where the substance of the case lies…[221]

Morality, Davies, argues best explains this difference in attitude, after all, neither party could point to clear, persuasive scientific evidence in their favour – but this is an issue that I will return to later. Thus, the precautionary principle is ultimately a political or value-based decision making tool, regardless of the number of scientific assessments a precautionary regime might insist upon.

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[218] George Gaskell and others, 'Europeans and Biotechnology in 2010 Winds of Change?' (European Commission - Directorate-General for Research 2010) Eurobarometer 73.1 <http://ec.europa.eu/research/swafs/pdf/pub_archive/europeans-biotechnology-in-2010_en.pdf> accessed 1 April 2015; George Gaskell and others, 'The 2010 Eurobarometer on the Life Sciences' (2011) 29 Nature Biotechnology 113.

[219] 'European Communities – Measures Affecting the Approval and Marketing of Biotech Products' (n 206)

[220] G Davies, 'Morality Clauses and Decision-Making in Situations of Scientific Uncertainty: The Case of GMOs' [2006] Hebrew University International Law Research Paper No. 10-06 250 <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=920754> accessed 1 April 2015.

[221] Ibid.

2.4.3 Products versus processes

When it comes to GMOs, what is it that we are being cautious about? What is the subject of moral and political suspicion? Is it the finished product in itself? Or is it the process required to create the finished product? It is important to observe that plants can be, and indeed are, modified through conventional breeding methods as well as through genetic engineering. In Europe, only crops that are created using genetic engineering technology are subject to rigorous regulations. The regime has been characterized as 'process-based' rather than 'product-based'.[222] Implicit in this is the perception that genetically modified plants are *more* dangerous to human health than conventionally or alternatively bred plants. To date, there is no evidence of harm to human health (death or illness) caused by either method of plant modification. If in fact a GM plant variety proved dangerous to human, animal or environmental health, surely the same plant produced conventionally or alternatively, would pose the same risk?[223] Yet, other breeding methods are spared the regulatory gauntlet. To some extent the regulatory treatment of GMOs reinforces an attitude of precaution towards GMOs.[224] On the other hand, the asymmetric regulation of modified plants undermines the European regime. If (conventionally) modified plants are permitted, and to date, have been safe, why regulate one method and not the other? Morris and Spillane argue that the EU actually misapplies the precautionary principle by regulating processes rather than products:

> 'Instead, we argue a more appropriate regulator framework, which would more logically reflect the idea of the precautionary principle, should focus on comparatively assessing the potential environmental and health risks versus benefits of a product, rather than overly focussing on the process through which the product…was created.'[225]

Others have expressed the same criticism of European policy in terms of discrimination.[226] Regardless of whether one agrees with the precautionary approach,

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[222] SH Morris and C Spillane, 'GM Directive Deficiencies in the European Union' (2008) 9 EMBO reports 500.

[223] Editorial, 'GM Faces Unfair Regulation in Europe - New Scientist' [2009] *New Scientist* <http://www.newscientist.com/article/mg20126943.700-gm-faces-unfair-regulation-in-europe.html> accessed 29 March 2015; Andy Coghlan, 'Conventional Crop Breeding May Be More Harmful than GM' [2009] *New Scientist* <http://www.newscientist.com/article/mg20126944.800-conventional-crop-breeding-may-be-more-harmful-than-gm.html> accessed 29 March 2015.

[224] See section 2.4.2

[225] Morris and Spillane (n 222).

[226] Ingo Potrykus neatly summarises the argument thus:
More defensible — on scientific and humanitarian grounds — and more practical would be for new genetically modified crops to be regulated, not according to how they are bred, but according to their

these inconsistencies call into question the internal logic of the European regulatory regime.

2.4.4 Exporting the precautionary principle/approach

Precaution, therefore, is well established within the EU, both in public opinion, and within the Administration. However, the European Union is not the only context in which the precautionary principle is embraced. If one observes the current international regulations, it is clear that the precautionary principle has a stronghold internationally too: the Cartagena Protocol iterates and reiterates the precautionary principle. Article 22 of the Protocol imposes a duty upon parties to co-operate with capacity-building.[227] However well-intentioned this obligation may be, it effectively exports and establishes the precautionary principle around the world. There is immense political – even moral - pressure to sign to international agreements such as Cartagena Protocol or the Kyoto Protocol. Many developing nations may lack the resources to develop and implement their own regulatory framework on issues such as GMO, which require expertise and equipment. The promise of capacity-building assistance, coupled with the political pressure to become a signatory to a well-regarded international agreement, is highly persuasive. International organisations such as UNEP, the World Bank, and FAO as well as governments, NGOs and private enterprises have all assisted in capacity-building under Cartagena, resulting in numerous nations developing their national frameworks in accordance with the precautionary approach. This comment is not intended as criticism of those nations who accept assistance – perhaps all things being equal they would opt to follow a precautionary approach anyway – rather as explanation of the wide-reach and stability the precautionary principle has gained.

However, the question I ask is this: notwithstanding any of the arguments in favour of the precautionary principle, is it universally relevant? Or even clear? Should we expect all nations to operate a regime of precaution? Is this realistic? In short, can we *all* afford to apply the precautionary principle? The precautionary approach may well suit European nations; putting aside all ethical arguments for and against GMOs, developed nations can *afford* to apply the precautionary principle. I submit that priorities might be different for nations who struggle to provide adequate nourishment for their own

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novelty, as are new drugs. All traits, however introduced, should be classified by their putative risk or benefit to the consumer and to the environment.
(Potrykus, 'Regulation Must Be Revolutionized' (n 131).

[227] Cartagena Protocol (n 163), article 22

people, whose political structures and economies are unstable, and whose agri-business are periodically crippled by climate conditions and natural disasters. For these nations GM technology may well provide the solution to a multitude of problems through enabling stronger, resistant, fortified and plentiful crops, and hence forcing one to reconsider the merits of precautionary approach in light of context.

The Cartagena Protocol's commitment to capacity-building is ultimately a commitment to the precautionary principle. It is certainly true that issues pertaining to environmental protection or biodiversity are global issues that by their nature transcend territorial parameters. Yet, these international concerns must be considered alongside the competing interests of sovereign nations. These issues are contextualized and discussed in the following section.

Golden rice, having been developed in Europe, is subject to the European regulatory regime described above. The inventors and supporters of Golden Rice have been remarkably vocal and firm in their critique of the EU authorisation process, which they deem lengthy, onerous and unnecessary. In a recent presentation Potrykus pointed out that: 'The outstanding challenge for the humanitarian Golden Rice project was GMO-regulation. It delayed deployment for more than ten years!'[228] Table B is a timeline of the Golden Rice Project to date, while table C breaks down in further detail the amount of time dedicated to jumping through the proverbial regulatory hoops.

[228] Ingo Potrykus, 'Genetic Modification with Plants: Unreasonable Regulation Prevents Public Good Projects' (Reason and Unreason in 21st Century Science, Christ's College, University of Cambridge, 11 December 2011).

TABLE B: Timeline of the Golden Rice Project [229]

1991 Beginning of PhD thesis.

1999 Proof-of-concept: biosynthetic pathway for provitamin A can be engineered into rice endosperm.

2000 Product development/regulatory conditions. Ex-ante studies. Event-independent regulatory data. Variety development.

2008 „lead event" for all subsequent breeding.

Continuation variety development. Data for regulatory dossier. Bio-availability. Social marketing. Seed multiplication.

2013 Variety registration. Deregulation. Release in Philippines.

2014 Bangladesh;

2015 Vietnam, India;

2016 China, Indonesia.

Further countries in Asia, Africa, Latin America to follow.

TABLE C: Time spent by Golden Rice Project on the regulatory process [230]

Deletion of selectable marker:	2 years
Screening for streamlined integration:	2 years
Screening for regulatory clean events:	2 years
Protection against liability problems:	3 year
Transboundary movement of seeds:	2 years
Obligatory sequence greenhouse-field:	1 year
Permission for working in the field:	8 years
Requirement for one-event selection:	2 years
Experiments for the regulatory dosier:	6 years
Deregulation procedure:	1 year

Underlying all this is a deeper criticism of the impact the European regulatory framework has outside the European Union. The WTO case between the US, Canada and Argentina, and the EC clearly revealed the implications and effects of European policy on international trade-relationships. There is perhaps not a great deal of sympathy for disrupted trade between Europe and developed Western countries such as

[229] Ibid.
[230] Ibid.

America and Canada. However, these countries are not the only ones to feel the impact of European policy and regulations – an impact which is perhaps much more palpable in the context of a product such as golden rice and its intended beneficiaries.

In 2003 the Nuffield Council on Bioethics published their report on 'The use of genetically modified crops in developing countries – a follow up discussion paper'.[231] In this paper, the Nuffield Council point out the impact the EU regulatory framework has internationally, specifically in relation to developing nations. Firstly, developing countries that wish to export crops to the EU will be influenced by the list of crops already approved by the EU. Secondly, these nations are unlikely to be able to cope with the burden of risk assessments, safety tests, labelling, traceability and monitoring requirements the European regime demands, for these require financial and professional resources, as well as functioning institutions and systems already in place. These regulatory measures will prove most challenging for poorer, small-scale farmers:

> 'Many small-scale farmers in developing countries grow crops for export such as sugar, coffee, tea, rubber and cotton. Small-scale farms are run by much poorer people, and employ considerably more workers per hectare than large plantation- based farms. It is therefore especially important that developed and developing countries avoid measures that discriminate against these small-scale growers.'[232]

Thirdly, developing nations who wish to produce GM crops for domestic use, as well as non-GM crops for export will face the same labelling and traceability difficulties, as well as the added task of ensuring (insofar as it is possible) separation of crops. The risk of 'crop-contamination' essentially forces nations to choose between producing to feed their own population and producing to export. Finally, the attitude and outlook of European consumers and European institutions is powerful:

> '…if the current perception of the majority of European consumers that such imported materials are 'contaminated' prevails, it is very likely that GM food and feed, and products derived from GM crops, will be less competitive on European markets.'[233]

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[231] Nuffield Council on Bioethics, 'The Use of GM Crops in Developing Countries: A Follow-up Discussion Paper' (2003). This is follow-up discussion paper to the original report: Nuffield Council on Bioethics, 'Genetically Modified Crops: The Ethical and Social Issues' (1999).
[232] Nuffield Council on Bioethics, 'The Use of GM Crops in Developing Countries: A Follow-up Discussion Paper' (n 231) 81.
[233] Ibid.

The report continues:

> 'Unless European consumers become far less sceptical towards GM crops, few developing countries will wish to grow them. We have observed that a rapid spread of GM crops has already occurred in several parts of the world (paragraph 3.21). However, scarcely any GM food and feed crops have been approved for commercial planting in the developing countries of Asia, Africa or the Middle East. This situation appears to derive in part from fears that a highly restrictive interpretation of the precautionary approach in Europe and Japan will close off export sales.'[234]

It goes without saying that sovereign states reserve the right to self-determination. Countries should be free to grow, buy and sell produce as they wish, be it GM, conventional or organic. But, most countries also have a number of international obligations; even if a country wishes to keep its legal obligations to a minimum, as part of the global community there are issues of global concern that cannot be ignored. In this context two competing interests (ultimately translated into conflicting regulatory regimes) are at play: Firstly, as cross-pollination between plants cannot be contained *regardless of whether they are genetically modified or not,* the threat to biodiversity and environmental protection has been pushed as a global issue, which arguably transcends national interests, by politicians, interest groups, lobbyists and the media. On this point, it could be argued that genetic modification encourages, rather than threatens, actual and potential biodiversity; by creating new plant species genetic modification adds to the sum total of species in the environment.[235]

Secondly, inter-dependence vis-à-vis trade is also a global issue. The effects of national policy are felt on a global scale:

> 'The freedom of choice that farmers in developing countries can exercise is severely restricted by the agricultural policy of the EU. This policy has been developed primarily to protect European consumers and the environment from potential dangers. But after almost a decade of use of GM crops, there is no

[234] Ibid 81–2.

[235] I am grateful to John Harris (Lord Alliance Professor of Bioethics and Director of the Institute for Science, Ethics and Innovation, University of Manchester) for this point.

> robust scientific evidence that their consumption has adverse effects on human health…'[236]

Inherent within this critique is the question of when precaution ceases to be relevant. Theoretically, precautionary regimes are subject to on-going review[237] so the question of whether precaution is necessary ought to be omnipresent. Reality may be different. As relates to GMOs, the answer is not readily forthcoming as i) the invocation of the precautionary principle might be politically rather than scientifically inspired and ii) the acknowledged scientific uncertainty means we are lacking 'hard' evidence. Food security, economic stability, eliminating poverty and ill-health throughout the developing world, are issues that are equally as important as biodiversity. These competing issues demand the same level of consideration within a global context by both international organizations and nation states. Genetic modification may or may not provide the solution to these problems but countries ought to have the freedom of choice to use this technology.

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[236] Nuffield Council on Bioethics, 'The Use of GM Crops in Developing Countries: A Follow-up Discussion Paper' (n 231) 82.

[237] Schomberg writes: 'Precautionary measures are provisional measures by nature, and need to be regularly reviewed when scientific information either calls for relaxation or strengthening of those measures.' Schomberg (n 211) 34.

2.5 An alternative approach to global GMO regulation

2.5.1 Re-examining regulatory goals and an alternative structural approach

The issues enumerated above refer to the impact of EU GMO policy on trade and domestic production. Golden rice demonstrates the impact of EU agri-policy on a different level. Golden rice was produced and refined with the sole purpose of humanitarian aid. Despite being developed within Europe, the intended beneficiaries of this product were never within European consumer pool. Rather the inventors saw a way of providing much needed pro-vitamin A to rice-dependent communities in the developing world and sought to do so. As the product was developed in Europe, the inventors were bound by the European regulatory regime, like any other producer/manufacturer of a GM product. There is nothing unusual in this – consistency and universality in application are seen as marks of a 'good' modern regulatory regime.[238] Equally important are the results produced by the regime. In light of the unsatisfactory regulatory experience of the Golden Rice Project and the effects thereof, it is necessary to consider the alternatives.

For the sake of clarity, I should point out that as the legislative reviews[239] discussed in the preceding section show, there is actually very little serious institutional dissatisfaction with the regulatory regime. In fact, on the whole the regime is seen as theoretically sound, albeit flawed in execution, and therefore functioning relatively *well*. Although improvements were recommended,[240] they were minor changes; nowhere was wholesale regime change suggested. The dissatisfaction with the regime expressed here stems from studying the golden rice experience. One option would be to, as Potrykus suggest, 'revolutionize' the regulatory regime altogether, to wipe the slate clean and start over. However, attitudes are much slower and more difficult to alter than statute books. Given the culture of precaution now familiar within Europe at present this is, I contend, simply unrealistic. A more realistic option is to adopt a multi-layered, context-dependent approach to regulating GMOs both from within the European Union and

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238 Better Regulation Task Force, 'Principles of Good Regulation' (n 14). Following the 'Better Regulation' movement, 'good' regulation is characterized as transparent, accountable, proportionate, consistent and targeted.

239 European Commission - Directorate General for Health and Consumers and others (n 190); European Policy Evaluation Consortium, GHK Consulting and Technopolis (n 190).

240 European Commission - Directorate General for Health and Consumers and others (n 190); European Policy Evaluation Consortium, GHK Consulting and Technopolis (n 190).

internationally – 'regulatory differentiation' and 'streamlining regulation' alluded hitherto – and it is to this that I will turn my attention.

First however, it is necessary to briefly examine some structural features of the pre-existing framework. Regulatory theorists and commentators have long been discussing the various merits and demerits of regulatory competition versus regulatory harmonisation – and all the options in between.[241] Both the European Union framework on GMOs and the Cartagena Protocol are examples of regulatory harmonisation. Given the cross-border complexities of this issue there are good arguments in favour of harmonisation, both theoretically, and in the specific context of GM regulation. Both the EU and Cartagena frameworks emphasize precaution as the risk regulation method of choice, and as previously discussed implement this comprehensively. Whilst the global character of this issue instinctively points one in the direction of harmonisation as the most appropriate regulatory approach, I suggest an alternative approach. I contend that harmonisation is the *easiest* method of regulating in this field – however, it is not necessarily the most appropriate.[242]

The harmonised regulatory structures currently in place focus exclusively on protecting a particular sort of biodiversity at the expense of trade-related interests. As previously noted, for many nations these interests are not simply financial interests but are closely intertwined with issues such as food security and poverty alleviation (although, the importance of economic stability should not be underestimated).[243] I maintain that these interests are equally as important, and ought to be reflected in the choice and implementation of regulatory mechanisms. Fundamentally, the interests and priorities

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241 DC Esty and D Geradin, 'Regulatory Co-Opetition' (2000) 3 Journal of International Economic Law 235; AO Sykes, 'Regulatory Competition or Regulatory Harmonization? A Silly Question?' (2000) 3 Journal of International Economic Law 257; Baldwin, Cave and Lodge (n 3) chapter 17; Charles M Tiebout, 'A Pure Theory of Local Expenditures' (1956) 64 The journal of political economy 416; Claudio M Radaelli, 'The Puzzle of Regulatory Competition' (2004) 24 Journal of Public Policy 1; Steven K Vogel, 'International Games With National Rules: How Regulation Shapes Competition in "Global"Markets' (1997) 17 Journal of Public Policy 169; JP Trachtman, 'Regulatory Competition and Regulatory Jurisdiction' (2000) 3 Journal of International Economic Law 331; William W Bratton and Joseph A McCahery, 'The New Economics of Jurisdictional Competition: Devolutionary Federalism in a Second-Best World' (1997) 86 Geo. LJ 201; JP Trachtman, 'International Regulatory Competition, Externalization, and Jurisdiction' (1993) 34 Harv. Int'l. LJ 47.

242 In certain contexts, harmonization is appropriate. In chapter III I set out an argument in favour of harmonized international regulations on operational matters pertaining to international stem cell research; see in particular 3.2.1, 3.4. Likewise, in chapter IV agreed screening protocols within the international gene synthesis industry is welcomed (see 4.4, 4.5). What distinguishes the situations discussed in chapters III and IV, with the GMO situation is context – see 5.2.1.

243 Of course these trade-related interests are not confined in favour of developing nations: perhaps some countries within the EU would benefit from cultivating or importing GMOs.

of nations will not be the same; the interest and priorities of a developed Member State of the EU will differ greatly from those of a developing country in South-East Asia. As such, regulatory frameworks ought to be sensitive to these differences and designed according to specific context.

Here, I wish to introduce the idea of *streamlining* regulations, and drawing a distinction between this and a traditional concept of harmonised regulation. Streamlining certain elements of policy/process/standards across competing and/or distinctive regulatory systems offers an alternative method to balance and address competing interests and common ground. Allowing nations or regions to design and implement regulatory frameworks according to their own interests, will result in a degree of regulatory competition – countries will opt for the strategy and mechanisms that best serve their own interests, and these will not necessarily be the same. However, this does not mean that global or collective concerns must be altogether ignored within the structure of each regime: it is possible for nations to co-operate and agree on certain key issues (say, protecting endangered species or maintaining a species register) without insisting upon a regulatory approach and structure that might not suit everyone (e.g. the precautionary approach). 'Competing' regulatory systems can be streamlined where necessary. So, for example, it is possible to agree that any scientific data or test results be presented in the same format or deposited in a particular database for ease of reference and so forth, creating smoother administrative procedures.[244] Albeit not a legally binding document, the Codex Alimentarius is an example of 'streamlining' in the field of food safety standards. The approach I offer here is not the golden formula that will happily resolve all tensions and problems. There will still be contentious issues that necessitate a difficult conversation and compromise, for example, negotiating an acceptable threshold level of 'contamination' between GM and non-GM plants. For, given GMOs exist and are cultivated, and given we cannot control the earth's atmosphere, *some* cross-pollination will occur/has already occurred. Therefore, the question is not binary in nature, but one of degree. Streamlining regulation as outlined is a pragmatic, yet flexible approach that accommodates differences in policy and procedure, and also supports elements of commonality across regimes where necessary.

[244] For an extended exposition of this argument see 3.2.1 and 3.4 on harmonizing operational standards in international stem cell research.

Underlying this approach is an acknowledgment that harms and benefits are relative: what is harmful to one community may be beneficial to another. The complexity of these competing interests must be managed rather than sidelined, trampled upon, or simplified. Accordingly, regulatory standards will differ depending on context. In other words, the results of a cost-benefit analysis vis-à-vis any given product will be contingent on context-specific factors.

This leads me to two conclusions. Firstly, a unified, global approach to GMOs that serves everyone's interests is impossible to achieve.[245] Jurisdictional competition in policy and regulatory structure is inevitable, but this situation is hardly novel and nation states have differences of opinion on many issues from human rights to taxation. Secondly, given the importance of context (see further 5.2.1), there is an argument for alternative regulatory standards for GMOs depending on the product and target market. If we accept that a cost-benefit analysis will produce varying results depending on context, it follows that when formalizing the said cost-benefit analysis through regulation, standards should be contextualized accordingly. To a large extent, this argument is propelled by the need to look at outcomes of a regulatory regime.[246]

Returning to the golden rice case study, although it was developed in Europe, the intended beneficiaries of golden rice are not within Europe. Yet this product was subject to standards relevant for the European market. The result of this is a lengthy delay in this product reaching the target market, which questions the ethics and efficacy of the regulatory regime. For a single mother living in poverty in the slums of Dhaka, the potential risk of harm to human health from GMOs, is not likely to carry much weight, against the benefit of feeding herself and her child rice containing much-needed pro-vitamin A. A single mother living in a developed European country might afford the same potential harm a little more weight as a) vitamin A deficiency is less likely in the first place, and b) there are likely to be available alternatives to obtaining sufficient pro-vitamin A.[247] That is to say, what constitutes an adverse cost-benefit rationale will

[245] Similarly, as argued in chapter III, a international ethical consensus is difficult to achieve in the context of stem cell research; see 3.2.1, 3.3, 3.4

[246] On the matter of *ethical* outcomes see 1.3, 5.2.4

[247] I acknowledge that one response to this scenario is to ensure that the alternative methods of obtaining a sufficient amount of pro-vitamin A be made available to the single mother living the slums of Dhaka. However, that is the subject of a separate discussion outside the scope of this chapter. At present, golden rice is offering a solution (that may be partial and/or temporary) to the issue of vitamin A deficiency, which ought to be considered.

differ according to circumstances. Concerns for safety are important, but, *beyond the minimum standard*, the price of safety must be assessed according to context, and competing interests. Safety does not come at a 'fixed price' – the point at which something becomes 'worth the risk' is likely to be different according to circumstances. By this, I mean that many lifestyle decisions are left to individual discretion vis-à-vis safety and risk. A person who engages in extreme sports or smokes cigars assumes more risk and has a different personal safety standard than their counterparts who do not engage in such activities. The same discretion can be applied to GMO cultivation and consumption across nation-states; based on current evidence and experience, the risk-evaluation reveals that consuming GMOs is not particularly high risk for anyone.

It is important to emphasize that I am not suggesting governments apply different standards according to geographic region or populations, rather standards ought to be relevant and *appropriate to the target market or intended beneficiaries* (and this may or may not be geographically determined) as well assessing risk-absorption on a cost-benefit spectrum. This style of regulation, which I term 'regulatory differentiation', is not the equivalent of affirmative action or two-tier systems. Rather, it is acknowledging that after a minimum level of safety and quality assessment has been met, i.e. a product is either safe for everyone or no-one at all (in the case of GMOs this can be assumed as having been met as the EU have authorised a number of GMOs[248]), the standard adopted serves the target market or intended beneficiaries' interests (or any other regulatory goal). Hence, one might produce pro-vitamin A enriched rice aimed at vitamin-A deficient, rice-consuming populations, and iron-enriched red kidney beans or spinach aimed vegetarian and vegan populations, and so on. Of course, both target markets and consumers retain freedom of choice as to whether they produce and consume the product or not – but the choice should be available.

At present there is no alternative track for products aimed at a different market, with different concerns (medicinal or ethical claims) - products such as golden rice. I suggest that perhaps there ought to be. Regulatory differentiation can be applied to produce a regulatory framework that is *nuanced* through implementing a multi-layered, multi-track approach that takes account of context. Regulation is a tool to achieve specific outcomes, and regulatory regimes only make sense when analysed within the context of

[248] 'EU Register of Authorised GMOs' (n 177).

their application. Regulatory differentiation, together with regulatory streamlining across common interests and obligations, more accurately reflects the complexity of regulating this field. Admittedly, it is not simple to construct or easy implement – but neither are the issues provoked by the biotechnology in question.

2.5.2 Allocating regulatory space for ethics

Throughout this chapter I have suggested that the European regulatory regime fails to allocate adequate regulatory space to ethical and social concerns, focussing instead on scientific assessment. I will now explore this contention more closely. The process of genetic modification involves complex science, and it follows that regulating this technology will invariably involve scientific assessment. However it is not the only assessment that carries weight: technologies have a social impact as well as a material-scientific impact. Thus, the regulatory process must take into account and accommodate concerns of a social and ethical nature. At this point, it is worth stepping back to assess the interaction between ethics and regulation.

In order to know how to act – in this case whether or not to allow cultivation, consumption and transboundary movement of genetically modified organisms – we need to know many things. We first need reliable information as to whether there are safety issues for consumers. This can only be understood when possible dangers of consuming Golden Rice are balanced against possible dangers of not doing so, for all possible consumers. In part this will involve uncovering the relevant parties' interests, rights and responsibilities and where they might conflict. But we also need to think about what alternatives might be available to meet all those interests, respect those rights and discharge those responsibilities. In other words, we need to ascertain tensions and potential effects (both good and bad) of a course of action. To do this, we look to ethics. An ethical inquiry will hopefully elucidate any difficulties and help clarify aims. This is the starting point for developing a sensible, workable regulatory framework. The outcomes of an ethical discussion will contribute towards informing the substantive content and direction of a regulatory regime – and therein lays the interface between ethics and regulation. Ethics sets the parameters, the limits for the regulatory regime. In this sense, its role is in the 'pre-regulatory' or 'pre-law' stage. Ethics tells us the 'ought', which is then implemented through a variety of regulatory techniques.[249]

[249] See also 1.3

Of course, ethics is not the only field that will contribute towards the substantive content of a regulatory regime; economics, political science, pre-existing law, sociology, and of course science (this is not an exhaustive list of relevant disciplines), will all feed into it. In the case at hand, these concerns are intricately linked to one another and investigating the 'ought' will force one to consider issues beyond the field of pure ethics. Regulatory theorists can then construct an appropriate form of regulation to accommodate the demands of these diverse contributions in so far as is judged necessary.

The Cartagena Protocol and the European regulatory framework were developed and implemented when genetic modification was a relatively new technology. Little was known about the technology itself or the effects of the technology on the environment, human health or animal health. In a climate of apprehension about 'Frankenstein foods' it is hardly surprising that a conservative formulation of the precautionary principle was adopted. Although the state of scientific knowledge has improved over the past decade, it is true that science cannot predict with accuracy long-term effects of this technology. However we have had the benefit of experience – and to date, those experiences have not been harmful.[250]

Throughout this chapter I have indicated, implicitly if not explicitly, some of the tensions and competing interests that are relevant to genetic modification. In truth, despite clear allegiance to the precautionary principle, the current regulatory framework is unsatisfactory from whichever perspective it is seen. For it neither whole-heartedly protects environmental concerns, nor does it embrace bio-progress, trade and development. Of course, pleasing all camps will be impossible, but the current framework appears wholly insensitive to the tensions and competing interests that surround the issue of genetic modification. Perhaps at its inception, when the practical impact of genetic modification was difficult to discern, precaution was an appropriate regulatory response. I suggest this is no longer the case. The facts are: GMOs *are* allowed to be developed, cultivated, imported, exported, used and marketed in consumer products within the EU's jurisdiction. The regulations simply make it difficult, time-consuming and expensive to do so (more so, given the cultivation

[250] This point underlines the importance of choosing the appropriate regulatory approach at the appropriate time; see 5.3.1

restrictions and prohibition powers now available to Member States under Directive 2015/412/EU), arguably without justification. These difficulties are now being transposed on a wider scale in terms of food security, poverty, economic stability, trade-relations and so forth. Given the regime is not committed to an anti-GM stance, and given the current and future wider impact of the regime, its integrity is now questionable. Even if the 'ripple effects' of the European regime were not intelligible at the outset, they are now, compelling a comprehensive review of the underlying ethics and goals of the regime. The real question for policy makers is: to what extent do we regulate this technology? In other words, where do we draw the line, and why? Answering that question demands probing the underlying ethics of the policy and strategy.

To be clear, the critique I offer here is not that the European regulatory framework is unethical*,* rather that it: a) fails to fully consider the ramifications of its policy which results in arguably unethical outcomes, b) that it affords no 'space' for socio-ethical risk-benefit analysis, and c) that had the framework allocated such space, the effects of regulation and policy would have an opportunity to be addressed. I have argued that the regulations fail to appreciate the broader humanitarian (and economic) impact of GMOs and European policy therein, and in this sense is socio-ethically obtuse. It is equally as plausible that someone else might argue the regulations fail to satisfactorily appreciate the potential risks of GMOs and scale of public concern, and in that sense is socio-ethically obtuse. In fact, the invocation of the national safeguard clause[251] is an example of the latter. The lack of regulatory space dedicated to socio-ethical assessment cuts both ways.

It is important to note that a socio-ethical inquiry is unlikely to return a single answer to the question 'what ought we do, and why?' Consensus is a rare thing in the field of emerging biotechnologies. Balancing competing interests and managing tensions is one of the challenges of developing regulatory frameworks in this field. Whether the issue is genetic modification, stem cell research, or synthetic biology achieving ethical consensus is likely to remain elusive. I contend that part of managing the absence of ethical consensus lies in both conducting a thorough consultation (involving all stakeholders as well as the public) during the 'pre-law' or 'pre-regulatory' stage, and allocating adequate

[251] See sections 2.3.1 'European Union regulations' and 2.3.2 'International regulations'

space within the regulatory framework for on-going discourse.[252] This is important for two reasons. Firstly, the complexity of this issue and different perspectives should not be ignored. Secondly, and following on from the first point, the world is not a static place. Interests and priorities change, science and social understanding are constantly advancing; good regulation will both acknowledge and be able to accept this.[253]

Thus, a harmonisation approach to regulating GMOs strikes as particularly peculiar. By impelling a specific policy and administrative approach, the complexity and nuance of this issue is overlooked. Regulatory policy cannot accommodate all socio-ethical concerns, however it can at the very least allow space to voice those concerns. Better regulatory frameworks will accommodate nuance through flexible processes. That is to say, by developing a multi-track or 'differentiated' framework that can take account of specific goals pertaining to GMOs, as well as broader, competing and common interests (the latter to be achieved through essential 'streamlining'). What emerges is a considerably more complex portrait of the regulatory landscape: competing national and/or regional regimes, ideally comprising a layered or multi-track (rather than single-track) system, but consistently integrating overarching international obligations within each regime.

These proposals do not necessarily give products such as golden rice an automatic green light. However, I suggest that the approach to regulation advocated here would provide a more suitable forum for assessment and authorisation of products such as golden rice. If, both regulatory policy and processes take account of socio-ethical and economic nuance, and a product such as golden rice is estopped or delayed, then that is the price we pay for good procedure. Just as election results or legal judgments cannot be contested simply because we do not agree with the result – recognized grounds of appeal, such as procedural impropriety, are required – so too with regulation. Hence, it is imperative that the regulatory procedures are thoughtfully, appropriately designed, for only then will they produce defensible results.

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[252] See 1.3

[253] Hence, the argument in favour of new governance (1.2.1), characterized by flexibility and adaptability put forward in chapters III and IV.

2.6 Conclusion

In this chapter I have advanced two distinct lines of critique pertaining to the regulation of GMOs, primarily within the current European framework. The first critique may be characterized as the 'external' or 'global' dimension of GMO regulation. I critically assessed the international impact of European agri-policy and parts of the international framework. Focussing on the predominant regulatory approach – 'precaution' – I discussed its (in)adequacy to absorb and address pertinent competing interests and views, and its impact thereof. The need for frank discussion of the competing interests at play – biodiversity versus trade-dependence versus trade interests versus poverty alleviation – and the need for a more accommodating, flexible framework cannot be overstated. The second strand of critique may be characterized as 'internal' or 'EU-focussed'. Here, I have argued that the current framework fails to allocate sufficient space for considerations beyond scientific reasoning required in the risk assessment procedure. Ethical, social and economic impact assessments are pushed outside the formal regime, resulting in a *partial* assessment of the products in question. This, I contend, is a fundamental failure of the regime, rendering it inadequate in the present, and ill-equipped to meet future challenges. By weaving the story of golden rice into my critical analysis, I hope that I have highlighted the socio-ethical (and to a lesser extent, economic) dimensions of regulating GMOs, and importance of taking these perspectives into account.

Whilst acknowledging that at present it is unrealistic to expect any real 'revolution'[254] (that is to say, move away from the current precautionary approach) in either the European or international regulatory regime, it is perhaps time to consider reform. It is encouraging that this important issue has re-emerged within the UK's political agenda and national media platforms. Creating regulatory space for socio-ethical concerns will allow products to be regulated in the full context of their potential use. This will facilitate communication and understanding between interested parties, and hopefully lead to a more nuanced, multi-layered approach to regulation, equally capable of acknowledging common ground and accommodating different perspectives.

[254] Potrykus, 'Regulation Must Be Revolutionized' (n 131).

CHAPTER III

Principles & Polycentricism: designing cross-border regulatory systems for stem cell research.

3.1 Introduction

Since the 1970's advances in stem cell research have inspired hope and ambition for the future of modern medicine.[255] It is anticipated that stem cell research will provide detailed insight into human development, enable accurate models of human diseases to be made in the laboratory in order to better study the disease progression, and lead to development of regenerative medical therapies.[256] Yet, the question of how best to regulate stem cell research remains an issue within contemporary politics and policy making. The rapid rate of progress and movement in this field is such that the regulation of stem cell research, and more specifically, identifying and applying appropriate governance mechanisms, continue to interest and challenge us.

However, the speed of technological advance is not the only, or even the primary, impediment to smooth, clear, and efficient regulatory processes. Stem cell research is an expanding field; research aimed at unlocking the potential of stem cells is taking place around the world both collaboratively and competitively, and stakeholders and interest groups are likewise dispersed.[257] Furthermore, research using human embryonic stem cells is ethically controversial, dividing both public and academic opinion.[258] How are we to regulate something that constantly challenges individual and collective moral philosophies? And, although stem cell research may promise to one day to cure the incurable, prevent the unpreventable, as yet it is still, simply a hope.[259] The future of

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255 'Timeline: A Brief History of Stem Cell Research' (*Science Progress*, 16 January 2009) <http://scienceprogress.org/2009/01/timeline-a-brief-history-of-stem-cell-research/> accessed 1 April 2015.

256 'Stem Cell FAQ' (*International Society for Stem Cell Research*) <http://www.isscr.org/home/resources/learn-about-stem-cells/stem-cell-faq> accessed 18 June 2013.

257 See 4.2 for a parallel argument in relation to international gene synthesis work

258 Andrew Siegel, 'Ethics of Stem Cell Research' in Edward N Zalta (ed), *The Stanford Encyclopedia of Philosophy* (Spring 2013, 2013) <http://plato.stanford.edu/archives/spr2013/entries/stem-cells/> accessed 1 April 2015.

259 Although note that there are a small number of clinical trials currently underway. See for example: Rachael Panizzo, 'Britain Trials Embryonic Stem Cells as Treatment for Blindness' (*BioNews*, 26 September 2011) <http://www.bionews.org.uk/page_107183.asp> accessed 1 April 2015; Nishat Hyder, 'Stem Cell Therapy for Autism Gets Clinical Trial Go-Ahead' (*BioNews*, 28 August 2012) <http://www.bionews.org.uk/page_169672.asp> accessed 1 April 2015; Ruth Retassie, 'US Stem Cell Company given Green Light for Blindness Trials' (*BioNews*, 6 February 2012) <http://www.bionews.org.uk/page_122942.asp> accessed 1 April 2015; Rosemary Paxman, 'Stem Cell

stem cell research is unknown and unpredictable. How are we to regulate an uncertainty? These difficulties are reflected in the current state of regulation pertaining to stem cell research at national and international levels.

This chapter focuses on the burgeoning international character of stem cell research regulation. (Although I acknowledge that there is a prior question of whether and why we ought to regulate this technology at all, that question is not tackled here.[260] I proceed from the position that regulating[261] stem cell research is an option to be explored.) Faced with complex issues of legality and the problematic interface between (bio)ethics and the design of cross-jurisdictional regulatory policy and frameworks, I look to 'new governance'[262] (NG) as an alternative to traditional, hard law, 'command and control'[263]

Transplants Hold Hope for Treating Blindness' (*BioNews*, 31 January 2012) <http://www.bionews.org.uk/page_120550.asp> accessed 1 April 2015; Nishat Hyder, 'Italian Government Orders Trial of Controversial Stem Cell Therapy' (*BioNews*, 3 June 2013) <http://www.bionews.org.uk/page_303600.asp> accessed 1 April 2015; Reuben Harwood, 'Japanese Pluripotent Stem Cell Trial Receives Ethical Approval' (*BioNews*, 18 February 2013) <http://www.bionews.org.uk/page_256910.asp> accessed 1 April 2015; Amina Aitsi-Selmi, 'First Trial of Synthetic Blood from Stem Cells on Horizon' (*BioNews*, 3 June 2013) <http://www.bionews.org.uk/page_306005.asp> accessed 1 April 2015; Matthew Young, 'Motor Neurone Disease Stem Cell Trial Advances to next Phase' (*BioNews*, 22 April 2013) <http://www.bionews.org.uk/page_286150.asp> accessed 1 April 2015; Rhys Baker, 'Japan's Health Ministry Approves Pluripotent Stem Cell Research' (*BioNews*, 28 June 2013) <http://www.bionews.org.uk/page_318150.asp> accessed 1 April 2015; Ana Ilic, 'Europe's First Marketing Approval for Stem Cell Product Granted' (*BioNews*, 2 March 2015) <http://www.bionews.org.uk/page_501176.asp> accessed 19 March 2015; Isobel Steer, 'Lung Cancer Stem Cell Therapy Gets UK Trial' (*BioNews*, 9 March 2015) <http://www.bionews.org.uk/page_503918.asp> accessed 19 March 2015; Lanay Tierney, 'First Stem-Cell Therapy Recommended for Approval by EU Regulator' (*BioNews*, 12 January 2015) <http://www.bionews.org.uk/page_483432.asp> accessed 19 March 2015.

[260] See 1.3

[261] I adopt a broad definition of the term 'regulation', embracing numerous conceptualizations of this notion as identified in Baldwin, Cave and Lodge (n 3) chapters 2–3. This encompasses this following: 'an identifiable and discrete mode of governmental activity'; 'sustained and focussed control exercised by a public agency over activities that are valued by a community'; 'a specific set of commands'; 'deliberate state influence'; 'all forms of social or economic influence'; and finally, as both a red light (restrictive) and green light (facilitative) concept. Simply put, I define regulation as attempting to change behaviour in order tackle a particular issue by using a particular tool, mechanism, practice or approach recognized within the academic discipline we know as 'regulation'.

[262] The term 'new governance' refers to a particular set of the regulatory approaches, mechanisms and procedures e.g. principles-based regulation. These approaches are non-traditional in that they are most easily defined by what they are *not* – traditional, command and control style regulation. See: Graínne de Búrca and Joanne Scott (eds), *Law and New Governance in the EU and the US* (Hart Publishing 2006); Scott and Trubek (n 9); Trubek and Trubek (n 8); Trubek and Trubek (n 9); De Burca (n 9); Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Cristie L Ford, 'New Governance in the Teeth of Human Frailty: Lessons from Financial Regulation' [2010] Wisconsin Law Review <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1525645> accessed 30 March 2015; Lobel, 'Renew Deal' (n 9); Lobel, 'Setting the Agenda for New Governance Research' (n 113); Sabel and Zeitlin (n 9); Black, 'Paradoxes and Failures' (n 40); Gráinne De Búrca, 'New Governance and Experimentalism: An Introduction' [2010] Wis. L. Rev. 227; Kenneth Armstrong and Claire Kilpatrick, 'Law, Governance, or New Governance-the Changing Open Method of Coordination' (2006) 13 Colum. J. Eur. L. 649; Burkard Eberlein and Dieter Kerwer, 'New Governance in the European Union: A

(CAC) regulatory solutions. More specifically, I advocate i) the use of 'principles' rather than 'rules' as a regulatory mechanism, and ii) embracing the reach and expertise of the growing network of international organizations concerned with stem cell research for the purposes of regulation. Hence, I propose developing a polycentric, principles-based regulatory regime for cross-border stem cell research.[264]

I will argue that in many respects a polycentric, principles-based regime is already in the process of organic development. For, in parallel to the trend towards cross-jurisdictional scientific collaborations in the field of stem cell research,[265] there are growing number of guidelines and consensus statements issued by non-governmental international organizations concerned with the operation of stem cell research globally.[266] I argue that these *regulatory collaborations* can be exploited as potential 'soft law' instruments. Thus, in this chapter I seek to define more precisely the nature of such activity within regulatory discourse by providing a conceptual and linguistic framework through which such soft law instruments and NG approaches can be developed, charted and assessed.[267] I argue that this is the optimal way in which the regulatory process ought to evolve in the field of biotechnology if we are truly concerned with developing progressive, ethically defensible international regulatory regimes.

At the outset I must clarify two important limitations to my argument. Firstly, this chapter advocates finding 'common ground' *where possible* between relevant actors in the field: research institutions, interest groups, industry, nations, regions, etc. The potential

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Theoretical Perspective' (2004) 42 JCMS: Journal of Common Market Studies 121; Scott, 'Regulation in the Age of Governance' (n 9). and 1.2.1

[263] This refers to the classic model of regulatory influence: orders/standards/commands backed by (legal) sanctions. See further: Baldwin, Cave and Lodge (n 3) 106 – 107.

[264] See 1.2.4

[265] See for example the following analyses of international collaborations in stem cell research: Sarah E Ali-Khan and others, 'Sino-Canadian Collaborations in Stem Cell Research: A Scientometric Analysis' (2013) 8 PLoS ONE e57176; Jingyuan Luo and others, 'International Stem Cell Collaboration: How Disparate Policies between the United States and the United Kingdom Impact Research' (2011) 6 PLoS ONE e17684; Jesse M Flynn and Kirstin RW Matthews, 'Stem Cell Research in the Greater Middle East: The Importance of Establishing Policy and Ethics Interoperability to Foster International Collaborations' (2010) 6 Stem Cell Reviews and Reports 143; Peter W Andrews and others, 'The International Stem Cell Initiative: Toward Benchmarks for Human Embryonic Stem Cell Research' (2005) 23 Nature Biotechnology 795.

[266] See 5.3.5

[267] Throughout this chapter I use the term 'soft law' (as opposed to 'hard law') in reference to the legal quality of an instrument, i.e. soft law documents are absent legally binding force; hard law documents possess such force. On soft law see 1.4.2 and 5.3.2

benefits[268] (academic and therapeutic) of stem cell research are too great to ignore; during these early developmental years collaboration, sharing research findings and ideas, open discussion and debate, can help focus, build and inspire research streams, reduce/avoid repetition, and ultimately maximize the chances of translating theory to therapy. One example of this type of collaboration is the on-going clinical trial involving patients with Stargardts's macular dystrophy at Moorfields Eye Hospital, London – a partnership between UK-based doctors and scientists, and the US biotechnology company, Advanced Cell Technology (ACT).[269] In September 2011 the UK's Medicines and Healthcare products Regulatory Agency (MHRA) approved this trial (the first clinical trial in Europe using embryonic stem cells), which is an application of a stem cell-based therapy developed by ACT.[270] In this context, collaboration and sharing is arguably as much pragmatic as it is noble or generous.[271]

Readers will note emphasis on the words 'where possible' in the first limitation stated above – this is an important qualification to the statement that bears further explanation. Encouraging the discovery of commonality between parties is by no means a call for wholesale policy and regulatory uniformity. Indeed, that would be both unrealistic and undesirable.[272] Sensitivities surrounding the status of the embryo means that complete ethical consensus in the field is, at present, impossible. Furthermore, the translation of a particular ethical position into policy and law might differ across nation states resulting in a variety of regulatory styles and regimes. This complicates the field certainly, but not necessarily in a negative way: regulatory competition (i.e. 'competitive adjustment of regulatory regimes in order to secure some advantage'[273]) can be a good thing.[274] Regulatory competition can encourage regulators to be responsive to their constituents' needs; it can offer choice and diversity of regime to constituents; it can incentivize innovation, and, by forcing researchers to explore different routes due to

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[268] 'Stem Cell FAQ' (n 256).
[269] Kate Doherty, 'Clinical Trials News: September 2011 Update' (*EuroStemCell*, 15 September 2011) <http://www.eurostemcell.org/story/clinical-trials-news-september-2011-update%20> accessed 1 April 2015; Kate Doherty, 'Clinical Trials News: January 2012 Update' (*EuroStemCell*, 13 January 2012) <http://www.eurostemcell.org/story/clinical-trials-news-january-2012-update> accessed 1 April 2015.
[270] Panizzo (n 259).
[271] On this point more generally see: John Sulston and Georgina Ferry, *The Common Thread: A Story of Science, Politics, Ethics, and the Human Genome* (Random House 2002).
[272] See chapter II for an example of the undesirability of an absolutely uniform regulatory approach in the context of international GMO regulation (2.4, 2.5), and the value in finding and streamlining commonality through regulation (2.5.1).
[273] Baldwin, Cave and Lodge (n 3) 356.
See generally: Ibid chapter 17.
[274] Tiebout (n 241); Radaelli (n 241); Vogel, 'International Games With National Rules' (n 241).

jurisdictional regulatory constraints, it can lead to new discoveries.[275] Notwithstanding the pre-conditions,[276] complexities and critiques of regulatory competition[277] the advantages enumerated above are all relevant to stem cell research. And, despite the moral pluralism prevalent in this field of research[278] there may be *some* matters (be they ethical or operational in nature) that can be agreed upon, and that might be useful to have agreement on in order to progress and fulfil the potential of this science. Finding that common ground, however limited, is what I encourage.

Secondly, although I expressly advocate principles-based regulation (PBR) through soft law documents as an effective method of regulating international collaborations in stem cell research, I do not advocate a blanket replacement of hard law with soft law, or 'command and control' with NG mechanisms for *all* dimensions of *all* stem cell research. Regulatory style, mechanisms and instruments must be suited to the activity and actors being regulated, the reach and expertise of the regulator, and the regulatory goals.[279] This might mean using only hard law or relying on soft law or a combination of both. Similarly it might mean opting for CAC, or a NG technique, or a combination of both. I term these combinations 'mixed model' regimes.[280] Those conducting stem cell research will likely be subject to a myriad of regulatory regimes (institutional, national, regional and international) shaping their behaviour from a variety of angles (criminal liability, civil liability, human rights, research ethics, intellectual property and so forth). They may be operating within both hard and soft legal frameworks, responding to both CAC and NG methods. Although traditional, CAC, hard legal frameworks are important and necessary in certain circumstances, they are not always the sole, most efficacious method of achieving the regulatory aims. NG mechanisms and soft law instruments can be exploited to 'fill in the gaps', complement or replace parts of the hard law framework. In fact, the benefits of each approach might even be best realized when they operate alongside each other.[281]

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[275] Baldwin, Cave and Lodge (n 3) Chapter 17.
[276] Tiebout (n 241).
[277] Radaelli (n 241); Trachtman, 'Regulatory Competition and Regulatory Jurisdiction' (n 241); Bratton and McCahery (n 241).
[278] See 1.3
[279] See 5.2.1, 5.3.1, 5.3.2, 5.3.3
[280] A mixed model can comprise any of the four elements. Although hard law/CAC and soft law/NG are more comfortable pairings, the inverse is equally possible. See also 1.3 on the technical neutrality of regulatory mechanisms.
[281] Black, 'Paradoxes and Failures' (n 40).

Complementarity between hard and soft law regimes, between CAC and NG, has been identified by others,[282] in particular when (re)considering the regulation and governance of biobanking[283] and the use of personal data for medical research.[284] Reflecting on the role and function of the law, Laurie notes its limits: a somewhat crude instrument, the law can clearly dictate what to do/not to do and settle disputes therein, but when faced with a decision-making dilemma, it is often unhelpful.[285] Here, a governance strategy can be helpful, for mechanisms such as reflexive governance[286] or principles-based regulation[287] provide a *decision-making methodology* based on *engagement* that is often absent in the inherent architecture of the law, traditionally characterised.[288] Here, I hope to demonstrate that a soft PBR regime can supplement hard, domestic legal frameworks to facilitate stem cell research and guide behaviour within the international dimension. I posit that the hard, legal architectures provide an essential starting point as citizens must know what they can/cannot do (e.g. under what conditions, if at all, is it legal to derive a cell line from a human embryo; under what conditions the cell line can be used for research, etc.). However, there are some matters that the law does not or cannot address (e.g. how to efficiently share data with laboratories outside one's own country), and here the development of principles to guide behaviour might be useful.

This chapter consists of six parts. I begin by briefly introducing and contextualizing 'principles based regulation' (PBR) and the applicability of this regulatory approach to stem cell research, citing the United Kingdom's Human Fertilisation and Embryology

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[282] Graeme Laurie, Shawn HE Harmon and Fabiana Arzuaga, 'Foresighting Futures: Law, New Technologies, and the Challenges of Regulating for Uncertainty' 4 Law, Innovation and Technology 1; Shawn HE Harmon, Graeme Laurie and Gill Haddow, 'Governing Risk, Engaging Publics and Engendering Trust: New Horizons for Law and Social Science?' (2013) 40 Science and Public Policy 25.
[283] Graeme Laurie, 'Reflexive Governance in Biobanking: On the Value of Policy Led Approaches and the Need to Recognise the Limits of Law' (2011) 130 Human genetics 347; Graeme Laurie, 'Consent as Contract: What Does Solidarity Tell Us about the Evolving Nature of the Consent Process in Health-Related Research?' (Solidarity: towards new solutions in the bioethics of biobanking; biosecurity; and health inequalities, Brocher Foundation, Geneva, Swizterland, 21 March 2013); Graeme Laurie and Emily Postan, 'Rhetoric or Reality: What Is the Legal Status of the Consent Form in Health-Related Research?' (2013) 21 Medical Law Review 371; Graeme Laurie and others, 'Managing Access to Biobanks: How Can We Reconcile Individual Privacy and Public Interests in Genetic Research?' (2010) 10 Medical Law International 315.
[284] Graeme Laurie and Nayha Sethi, 'Towards Principles-Based Approaches to Governance of Health-Related Research Using Personal Data' (2013) 2013 European Journal of Risk Regulation 43.
[285] Laurie, 'Reflexive Governance in Biobanking' (n 283); Laurie, 'Consent as Contract: What Does Solidarity Tell Us about the Evolving Nature of the Consent Process in Health-Related Research?' (n 283).
[286] Laurie, 'Reflexive Governance in Biobanking' (n 283); Laurie, 'Consent as Contract: What Does Solidarity Tell Us about the Evolving Nature of the Consent Process in Health-Related Research?' (n 283).
[287] Laurie and Sethi (n 284).
[288] Laurie, 'Reflexive Governance in Biobanking' (n 283); Laurie and Sethi (n 284).

Authority as example of a *national* principles-based regime (3.2). In section 3.3 I introduce the concept of polycentricity to the principles-based regulatory model; polycentricity enables the leap from disparate national regimes, to an international, inter-operable multi-organisational regulatory structure. Section 3.4 begins with an overview of the four modes of policy interoperability in the field of stem cell research classified by Isasi and Knoppers;[289] this forms an essential background to the regulatory design advocated here. I then identify key international regulatory collaborations (or instances of actual policy interoperability) that demonstrate the emergence of polycentric PBR. In section 3.5 I address some of the most pressing challenges of this type of regulatory regime poses: the impact of extra-territorial jurisdiction on the proposed regime, and the issues of legitimacy, accountability, compliance and enforcement. Here, another example from the UK, namely the UK Stem Cell Bank, illustrates standard-enforcing methodology that can be adopted internationally. Section 3.6 comprises my concluding thoughts on the development and future of an international stem cell research regulatory regime.

[289] Rosario M Isasi, 'Policy Interoperability in Stem Cell Research: Demystifying Harmonization' (2009) 5 Stem Cell Reviews and Reports 108; Rosario M Isasi and Bartha M Knoppers, 'From Banking to International Governance: Fostering Innovation in Stem Cell Research' (2011) 2011 Stem Cells International 1; Rosario M Isasi and Bartha M Knoppers, 'Mind the Gap: Policy Approaches to Embryonic Stem Cell and Cloning Research in 50 Countries' (2006) 13 Eur. J. Health L. 9; Rosario M Isasi and Bartha M Knoppers, 'Beyond the Permissibility of Embryonic and Stem Cell Research: Substantive Requirements and Procedural Safeguards' (2006) 21 Human Reproduction 2474; Rosario M Isasi and Bartha M Knoppers, 'Governing Stem Cell Banks and Registries: Emerging Issues' (2009) 3 Stem Cell Research 96; Rosario Isasi, Bartha M Knoppers and Geoffrey Lomax, 'Sustained Interaction: The New Normal for Stem Cell Repositories?' (2011) 6 Regenerative Medicine 783; Rosario Isasi and others, 'Disclosure and Management of Research Findings in Stem Cell Research and Banking: Policy Statement' (2012) 7 Regenerative Medicine 439; Bartha M Knoppers and Rosario Isasi, 'Stem Cell Banking: Between Traceability and Identifiability' (2010) 2 Genome medicine 73.

3.2 A principles-based approach[290]

It is not within the scope of this chapter to provide a detailed portrait of the operation and history of PBR.[291] However, some technical explanation as to the nature of principles and a principles-based regime is necessary in the interests of clarity. The rudimentary difference between rules and principles is perhaps best demonstrated through a simple example. A rules-based approach to controlling the environment of a classroom would perhaps dictate, 'the temperature must be maintained at 21 degrees Celsius, with a humidity level of 50%, and lit by three 100watt clear glass light bulbs'. A principles-based approach would simply say: 'the classroom must be well lit and maintained at a comfortable temperature and atmosphere'. Of course, within regulatory discourse the distinctions between the two are somewhat more subtle and sophisticated.[292] Principles-based regulation, therefore, is a mode of regulation that is led by loosely articulated objectives (i.e. 'principles'), as opposed to prescriptive rules, to guide behaviour. Julia Black, who has contributed significantly to the development of contemporary PBR in both theory and practice (certainly in the United Kingdom), characterizes PBR as two-dimensional. Firstly, a PBR regime can be either formal/rule-book or substantive (or indeed both). Secondly, the institutional setting of the regime can be either dyadic or polycentric (see 3.3). She summarises these dimensions thus:

> 'PBR can be formal, in the sense that there are principles in the rulebooks (including legislation, codes of practice and so on) but it may not be substantive. In contrast, a regime may have some of the operational characteristics of a PBR regime, but not have principles in the rulebooks. Where it is both, it is described as full PBR. Polycentric PBR is full PBR with the additional element that it is characterized by the enrolment of others, beyond regulators and firms, in the elaboration of the meaning and application of principles…These labels are not

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[290] See 1.2.4

[291] Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40).

[292] For an overview of the rules versus principles debate please see the following: Anand (n 43); Baldwin (n 43); Black, *Rules and Regulators* (n 43); Black, '" Which Arrow?' (n 43); Black, Hopper and Band (n 40); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Braithwaite, 'Rules and Principles' (n 39); Cunningham (n 43); Cristie Ford, 'Principles-Based Securities Regulation in the Wake of the Global Financial Crisis' (2010) 55 McGill Law Journal 257; Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Kaplow (n 43); Korobkin (n 43); Posner (n 43); Schauer, 'Convergence of Rules and Standards, The' (n 43); Schauer, 'Tyranny of Choice and the Rulification of Standards, The' (n 43); Sunstein (n 43).

> intended to have normative overtones; they are simply useful shorthand descriptions.'[293]

So, a principles-based regime can be described in terms of structure and/or content; the latter is qualitative in nature rather than prescriptive. Properly implemented, PBR establishes dialogue and engagement between the regulator and regulatee; here, regulation is a continuous and deliberative process of interpreting principles and critically assessing the application and behavioural responses thereof.[294] This necessary interaction between parties has numerous potential benefits: it can promote reflexivity, help build relationships between parties, open channels of communication, and develop knowledge and understanding between parties.[295] A dynamic process, PBR is inherently flexible and allows for more responsive and purposive regulation (again, properly implemented, this can be a highly efficient method of targeted regulation).[296] In the context of stem cell research, the flexibility offered by PBR can lead to a more facilitative regulatory environment that encourages innovation.[297] On-going dialogue between the regulator and regulatee (and indeed other relevant parties) enables scientific developments in this complex field to be better understood by the regulator, and therefore more sensitively and appropriately regulated.

Contrast the above to the draconian, pernickety, often antiquated rules of CAC[298] regimes that can encourage creative compliance ('gaming') and therefore distrust.[299] This kind of Utopian rhetoric is politically attractive and has much to do with the attention PBR has received.[300] As Julia Black says,

> 'The question of when to use rules, principles, or standards has also become a policy issue in its own right. In some policy areas, though by no means all, they have been recognised as being particular 'technologies' of regulation and as

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293 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40) 428.
294 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40).
295 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40).
296 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40).
297 Devaney, 'Regulate To Innovate' (n 52).
298 Baldwin, Cave and Lodge (n 3).
299 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40).
300 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40).

having particular properties, properties which policymakers in some areas have consciously sought to use and exploit for a variety of ends.'[301]

She continues:

'These monikers are more than just descriptions, however; they also carry significant normative content. Being 'rules-based' is usually denigrated as equating with nit-picking bureaucracy in which compliance with detailed provisions is more important than the attainment of an overall outcome. 'Principles-based', in contrast, evokes images of outcome orientated, flexible regulators harbouring ethical standards in largely responsible corporations.'[302]

Of course, the rhetoric of PBR must be swallowed with a large pinch of salt, for depending on implementation and institutional context, the inverse is just as likely.

Following the recent global financial crisis PBR has received considerable attention: in the UK the crisis was seen to indicate a failure of PBR,[303] whereas as in the USA it was the reverse, a failure of rules-based regulation and a prompt towards PBR.[304] Much has been written about the pros and cons of rules-based and principles-based systems (and indeed further alternatives): rules lend certainty, principles allow for flexibility, but then, rules are inflexible, principles lead to uncertainty and so forth. I do not propose to delve into this debate here as it is already well documented in the regulatory literature.[305] Similarly, engaging in a comprehensive, pre-emptive defence of PBR is outside the scope of this chapter, and indeed has been undertaken by others in the field.[306] The reader is asked to bear in mind that to date, no regulatory approach has proved itself flawless, and PBR is no exception. As Julia Black has written:

'PBR has the potential to live up the expectations of both its supporters and its critics, whether it does depends on how it is implemented and on the institutional context which surrounds it. Critically, that institutional context has

301 Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40) 2.
302 Ibid 3.
303 The Financial Services Authority (FSA) was one of the most vocal proponents of PBR, and seen worldwide as a 'leader' crafting PBR for financial services industry. See: Black, Hopper and Band (n 40).
304 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40).
305 On the rules versus principles debate see footnote 292
306 Black, Hopper and Band (n 40); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40).

to be characterized by the presence of a high degree of mutual trust between participants within the regulatory regime…'[307]

This chapter moves beyond the for/against or purely descriptive discourses on PBR to discuss the application of PBR in the context of international stem cell research.

Despite the battering PBR has taken post-banking crisis, for the reasons cited above it remains a contender amongst the various forms of regulation available to designers. Although the UK's former Financial Services Authority (the FSA has now been split into two separate regulatory authorities: The Financial Conduct Authority and the Prudential Banking Authority) has distanced itself from PBR, rebranding its approach 'outcomes-based' regulation (notwithstanding the public rebrand, little has changed on paper, for example, the former FSA's principles of business remain intact)[308] others are turning towards PBR now. Financial regulators in Japan and America are integrating PBR into their respective regimes,[309] and the Legal Services Board and Solicitors Regulation Authority in the UK have both opted for PBR.[310] Most pertinent for this chapter, the Human Fertilisation and Embryology Authority (hereafter HFEA) who oversee, among other things, stem cell research using human embryos and/or gametes has adopted PBR as part of its regulatory regime.[311] PBR is also the approach of choice for developing a voluntary Code of Conduct for research in nanotechnology.[312]

The great attraction PBR holds for the field of biotechnology is the flexibility and reflexivity it affords both the regulator and regulatee. Given the speed of scientific advance - which by far outstrips the speed of the political, legislative or litigation process - flexibility is key to effective, on-going regulation of current activity that is also ethically defensible. For example, technology to create human-animal admixed embryos

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307 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40) 426–7.

308Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40) 13; Financial Services Authority (n 49).
See also: Financial Conduct Authority, *Financial Conduct Authority Handbook* (2015) PRIN 1, 2, 3, 4; APER 1, 2, 3, 4 <http://fshandbook.info/FS/html/FCA> accessed 1 April 2015; Prudential Regulation Authority, *Prudential Regulation Authority Handbook* (2015) APER 1, 2, 3, 4 <http://fshandbook.info/FS/html/PRA> accessed 1 April 2015.

309 Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40) 3.

310 Ibid; Legal Services Board (n 51); Solicitors Regulation Authority (n 51).

311 Human Fertilisation and Embryology Authority, *HFEA - Code of Practice 8th Edition* (n 52).
Very little has been written on the HFEA's adoption of PBR, however see: Devaney, 'Regulate To Innovate' (n 52); Therese Callus, 'Ensuring Operational Compliance and Ethical Responsibility in the Regulation of ART: The HFEA, Past, Present, and Future' (2011) 3 Law, Innovation and Technology 85; Tony Prosser, *The Regulatory Enterprise: Government, Regulation and Legitimacy* (Oxford University Press 2010).

312 Insight Investment, Royal Society, Centre for Process Innovation, Nanotechnology Industries Association (n 53).

was established long before Parliament enacted legislation to regulate this technique. The Human Fertilisation and Embryology Act 2008 (amending the Human Fertilisation and Embryology Act 1990)[313] was passed 'after the event' in order to regulate *inter alia* the creation and use of human-animal admixed embryos for research purposes.[314] PBR as an adaptive mechanism will, I submit, go some way towards addressing this sort of regulatory 'lag' that often occurs in traditional, CAC systems of regulating biotechnologies.

3.2.1 The HFEA's PBR model

At this point, a brief survey of the HFEA's PBR model is apposite. Although this is a national, non-polycentric[315] PBR regime, it provides a practical example of PBR operating – arguably successfully – in the field of stem cell research. Section 8(1)(ca) of the HFE Act 1990 (as amended) requires the HFEA to 'maintain a statement of the general principles which it considers should be followed (i) in the carrying-on of activities governed by this Act, and (ii) in the carrying-out of its functions in relation to such activities'.[316] Following a consultation, the HFEA revised its Code of Practice and incorporated a set of thirteen principles into the Code. These principles are intended to reflect the HFEA's key regulatory priorities and indicate key behavioural practices and outcomes expected by the HFEA from each licensed centre; the principles inform every part of the Code of Practice[317]. So what do principles actually look like on paper? Here are the first three:

1. Treat prospective and current patients and donors fairly, and shall not discriminate against them unlawfully;
2. Have proper respect for the privacy, confidentiality, dignity, comfort and well being of patients and donors;
3. Have proper respect for the special status of the embryo when conducting licensed activities;
4. […][318]

These 'principles' set out general, broad ethical, behavioural standards that require the exercise of judgment from both the regulator and regulatee. These principles are not

313 Human Fertilisation and Embryology Act (n 54).
314 Human Fertilisation and Embryology Authority, *HFEA - Code of Practice 8th Edition* (n 52) 4A.
315 On polycentricism: see 3.3
316 Human Fertilisation and Embryology Act (n 54).
317 Human Fertilisation and Embryology Authority, *HFEA - Code of Practice 8th Edition* (n 52).
318 Ibid.

the sole guidance issued by the HFEA; the Code of Practice – a hefty document running to approximately 275 pages and continually being updated – contains detailed guidance notes (and a glossary), which cross-references the principles. In this context the principles-based regime is mandated by legislation or hard law and sits within the architecture of a traditional CAC style framework. This is a good example of a 'mixed-model', in which the CAC and NG structures develop to complement rather than detract from each other. Reflecting on the role of the 1990 Act, Sarah Devaney concludes:

> 'The utilization of primary legislation as a regulatory mechanism for this area was understandable in 1990…
>
> 'Two decades later however, and with the permissibility of such research and treatment being well established, it is right to supplement this with a more flexible regulatory mechanism.'[319]

The integration of PBR into this sphere of regulatory activity was relatively smooth and conflict-free, as Devaney has pointed out:

> 'This requirement [s 8(1)(ca) HFEA 1990] caused little disquiet in debates on the Human Fertilisation and Embryology Bill and its terms remained unamended throughout the Bill's passage through Parliament…
>
> 'Broad support was expressed by the respondents to the consultation for the Principles as drafted.'[320]

Similarly, post-implementation neither the principles themselves, nor the principles-based approach has been subject to serious critique. This is not for lack of opportunity to so do. The UK government's recent review of arm's-length bodies placed the spotlight on the HFEA (and its sister organization the Human Tissue Authority (HTA)), considering its functionality, operational efficiency and necessity as a regulatory authority. Yet, throughout the extensive debates and discussion, the HFEA's decision to employ PBR was not specifically criticized.[321, 322]

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[319] Devaney, 'Regulate To Innovate' (n 52) 59.
[320] Ibid 55.
[321] Human Fertilisation and Embryology Bill: Explanatory Notes to Bill versions HL Bill 6 – EN, 9 November 2007; HL Bill 70 – EN, 6 February 2008 and HL Bill 83 – EN, 24 October 2008.
See also: Edward White, 'Human Fertilisation and Embryology Bill - What Happened? - Commons Library Standard Note' (House of Commons Library 2008) SN/SC/4886 <http://www.parliament.uk/briefing-papers/SN04886/human-fertilisation-and-embryology-bill-what-happened> accessed 1 April 2015; Edward White, 'Human Fertilisation and Embryology Bill [HL] - Commons Library Research Paper' (House of Commons Library 2008) Research papers RP08/42 <http://www.parliament.uk/briefing-papers/RP08-42/human-fertilisation-and-embryology-bill-hl>

The HFEA's PBR model appears to have escaped wrath of academic commentators too. Tony Prosser[323] and Thérèse Callus[324] have recognized the principles-based approach in their respective critical evaluations of the HFEA's regulatory regime, yet neither writer subjects the PBR component to rigorous critique. Callus perceives the principles as accomplishing 'little more than the statutory requirements in the exercise of the activities authorized under the Act. The first principle is the only one which does not have an explicit statutory counterpart...'[325] Her commentary is not so much critical as it is dismissive of the role played by PBR within this regulatory scheme. While it is true that the principles set out in the Code of Practice reiterate legislative obligations, the important point here is one of regulatory methodology: PBR, as noted above, demands a very different, and arguably more attractive, *modus operandi* from both the regulator and regulatee, than CAC. Callus continues:

> 'The principles, the Code itself, are a functional method for setting standards and communicating these standards to those who are affected by the regulator. The emphasis upon this standard setting once again draws attention back to the

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accessed 1 April 2015; Edward White, 'Human Fertilisation and Embryology Bill [HL]: Committee Stage Report - Commons Library Research Paper' (House of Commons Library 2008) Research papers RP08/62 <http://www.parliament.uk/briefing-papers/RP08-62/human-fertilisation-and-embryology-bill-hl-committee-stage-report> accessed 1 April 2015; Elizabeth Shepherd, 'Human Fertilisation and Embryology Bill [HL] (HL Bill 6, 2007-08) LLN 2007/007 - Lords Library Note' (House of Lords Library 2011) Library notes LLN 2007/007 <http://www.parliament.uk/briefing-papers/LLN-2007-007/human-fertilisation-and-embryology-bill-hl-hl-bill-6-200708-lln-2007007> accessed 1 April 2015. Note the consultation documents in relation to the Human Fertilisation and Embryology Bill: Human Fertilisation and Embryology Authority, 'Response by the Human Fertilisation & Embryology Authority to the Department of Health's Consultation on the Review of the Human Fertilisation and Embryology Act' (2005) 05/33273 <http://www.hfea.gov.uk/docs/Review_of_the_HFE_act_response_to_may05.pdf> accessed 30 March 2015; Human Fertilisation and Embryology Authority, 'Review of the HFE Act - Preliminary Recommendations' (2005) <http://www.hfea.gov.uk/docs/Review_of_the_HFE_act_prelim_recomm_may05.pdf> accessed 30 March 2015; Department of Health, 'Review of the Human Fertilisation and Embryology Act: Proposals for Revised Legislation (including Establishment of the Regulatory Authority for Tissue and Embryos)' (2006) White paper, Cm 6989 <http://www.hfea.gov.uk/docs/Review_HFEA_Act_White_Paper_DH.pdf> accessed 30 March 2015; Human Fertilisation and Embryology Authority, 'Hybrids and Chimeras: A Report on the Findings of the Consultation' (2007) <http://www.hfea.gov.uk/docs/Hybrids_Report.pdf> accessed 30 March 2015.

[322] As a side note, both the HFEA and HTA were subject to independent review ('Fertility and Tissue Regulators to Be Reviewed Following Consultation' (*GOV.UK - Press releases*, 25 January 2013) <https://www.gov.uk/government/news/fertility-and-tissue-regulators-to-be-reviewed-following-consultation> accessed 30 March 2015.). The review concluded that the HFEA is to remain as an independent regulator ('HFEA to Remain as Independent Regulator of Assisted Reproduction' (*Human Fertilisation and Embryology Authority: Press releases and statements*, 17 July 2013) <http://www.hfea.gov.uk/7934.html> accessed 30 March 2015.)

[323] Prosser (n 311).

[324] Callus (n 311).

[325] Ibid 103.

> principal operational role that the HFEA is expressly mandated to carry out under the command and control model.'[326]

This point sits within a broader critique of the HFEA's failure to use 2008 reforms (that introduced 8(1)(ca) HFEA 1990) as an opportunity 'to address the ethical [as opposed to the operational] responsibility of the HFEA'.[327] Whether Callus would welcome a set of principles purporting to expressly address the HFEA's 'ethical evaluation and decision-making role'[328] is unclear – certainly, that would be a tall order as achieving ethical concord is as tricky in the UK as it is anywhere else.

Notwithstanding the apparent ambivalence towards the HFEA's PBR regime, by emphasizing its operational regulatory role, Callus highlights a crucial point: the importance of good operational regulation. The issue of how to regulate stem cell research is often dominated by controversial (bio)ethical debates – the moral status of the embryo, the definition of personhood, proprietary rights in human material, and so on.[329] Although these issues are hugely important, so too are the oft-overshadowed (arguably more mundane) operational issues of regulating stem cell research.[330] The operational role of regulation can be described as focussed on the smooth *functioning* of a regime; setting working standards, streamlining processes, ensuring consistency across the field etc., in short, providing the regulatory facilitation for the permitted activity in question to take place.[331] This is a significant part of regulatory activity that ought not be overlooked. Thus, a strong, clear, targeted operational regulatory infrastructure can be instrumental to the timely achievement of regulatory goals, and the development and progress of a sector. The HFEA's emphasis on its operational role through the mode of principles can therefore be seen as more significant and laudable than Callus implies; an example of a sector developing a more conversant and flexible regulatory regime. The operational side of regulation is particularly important – and somewhat more challenging - in the context of international (rather than national) scientific work and is an issue that I will return to in the following section.

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[326] Ibid.
[327] Ibid.
[328] Ibid 86.
[329] Siegel (n 258).
[330] The HFEA's regulatory functions can be distinguished as executive (i.e. operational) and advisory. See: Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52) Chapter 3.
[331] See 2.5.1

The HFEA experience demonstrates that principles-based regulatory oversight in the field of stem cell research is achievable – at least at national level. The question that dominates the remainder of this chapter is whether this method can operate on an international level, where multiple sources of regulatory authority, and a more densely populated field (regulators, regulatees, and other interest parties) complicate matters.

3.3 A polycentric structure

In this chapter I will transpose the principles-based method to the 'macro' or international level, which is a more relevant context for current and future trends in stem cell research. Moreover, I suggest that simply replacing 'rules' with 'principles' within a traditional characterization of what we conceive regulation to be, is to overlook not only the true contours of the regulatory landscape, but also the opportunity to develop the more sophisticated, nuanced regulatory frameworks that biotechnologies demand. This section explores the (potential) construction of an international principles-based regime, polycentric in nature. So: what is meant by 'polycentricism'? And why should we be concerned with the *international* dimension of regulation in this field?

Polycentric or decentred (I use these terms interchangeably) regulatory regimes are organizationally described as '[drawing] attention away from individual regulatory bodies, be they at the national or global level, and emphasiz[ing] instead the multitude of actors which constitute a regulatory regime in a particular domain'.[332] So, regulation is not necessarily 'imposed' from within a hierarchical structure by the State, several States, supra-States or indeed any other organization. Decentred regulatory systems can be conceptualized by five core characteristics: 'complexity, fragmentation, interdependencies, ungovernability, and the rejection of a clear distinction between public and private'.[333] This style of regulation 'emphasizes the existence and complexity of interactions and interdependencies between social actors, and between social actors and government in the process of regulation'.[334] Moreover, 'regulation is dialectical: both regulator and regulatee are at once autonomous of and dependent on each other'.[335] Finally, polycentric regulatory systems are hybrid in nature, involving both governmental and non-governmental actors, and multi-faceted in their strategic approach.[336]

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[332] Julia Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (2008) 2 Regulation & Governance 137, 6.
[333] Ibid 7; Julia Black, 'Decentring Regulation: Understanding the Role of Regulation and Self Regulation in a "Post-Regulatory" World' (2001) 54 Current legal problems 103.
[334] Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332) 7.
[335] Ibid.
[336] Ibid.

Thus, regulatory power is diffused and diversified, for regulation can be imposed or implied, by others or oneself, it can be legally binding or voluntary, hierarchical or lateral in origin and so forth. Biotechnology – specifically, stem cell research – is an international, often collaborative sector; scientific work travels and translates across borders.[337] Although national governments may compete to capitalize on scientific innovation, a number of international research initiatives have arisen in the field of stem cell research.[338] At the same time, governments, industry, interest groups, the media and civic society are becoming more engaged with the regulation and fate of biotechnologies *and with each other* (demonstrated through public engagement, media interest, vocal interest groups and political debate). As these various relationships develop and disperse, so too does the number of actors enrolled in business of regulating.[339] The act of regulating it is no longer limited to a simple, binary regulator-regulatee relationship, but performed by the myriad of actors that comprise a polycentric regime. Thus, the traditional conceptualization of regulation as a state-centred, rule-based, CAC style regime begins to fall apart. This presents a considerably more complex picture of regulation than a traditional top-down, CAC regime, or even a dialectical principles-based regime. One might ask, why complicate an already complicated picture?

Firstly, traditional modes of regulation – that is to say, legally binding, CAC systems – are not always achievable in the international context. There exists no international infrastructure for formal, hard governance of science on this scale, although some writers such as De Lorenzo,[340] have called for formal, legally binding regulation of science, in particular stem cell research. Nor, as I hope to demonstrate, is such an infrastructure or degree of formality necessary or even desirable for effective governance. This is for two main reasons. Firstly, the developing network of organisations with sector-specific expertise [341] provides a 'ready-made' regulatory

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337 See for example the following analyses of international collaborations in stem cell research: Ali-Khan and others (n 265); Luo and others (n 265); Flynn and Matthews (n 265); Andrews and others (n 265).
338 For examples of international research initiatives see footnote 265
339 Regulatory enrolment is one element of new governance; see further footnote 262, 3.4 and 5.3.4
340 Lesley N DeRenzo, 'Stem Cell Tourism: The Challenge and Promise of International Regulation of Embryonic Stem Cell-Based Therapies' (2010) 43 Case W. Res. J. Int'l L. 877.
See also: David B Resnik, 'The Need for International Stem Cell Agreements' (2004) 22 Nature Biotechnology 1207.
341 There is a growing body of literature from the field of Science and Technology Studies focussed on the role of the scientific expert. I do not intend this chapter or thesis to fall within that particular discourse; the word 'expert' here is used in its ordinary meaning. However, for a UK-focussed analysis of the role of the scientific expert in regulation of stem cell research see: Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52). More generally see the work of Sheila Jasanoff: Jasanoff, *The Fifth Branch* (n 36); Sheila Jasanoff, '(No?) Accounting for Expertise' (2003) 30 Science and Public Policy 157; Sheila

framework that might be exploited for these purposes (I will elaborate on this further below). Secondly, and following on from the first point, developing a formal, hard law framework from scratch is a lengthy, time-consuming and difficult task, the cost of which must be justified even if, as de Lorenzo suggests, we utilize pre-existing legal frameworks such as the United Nations.[342] I contend that taking such measures would be a gross overreaction to the issues presented by stem cell research, and inefficient use of 'hard' regulatory space and resources. For, the type/style of regulation must 'match' the activity and its incumbent risks,[343] it must be appropriate, apposite, and efficient.[344] Where there is a self-developing organizational network, arguably with the reach and expertise to regulate softly, why not exploit it?

Secondly, in order to fluently 'translate' and transfer data from stem cell research, for results to be universally meaningful to all scientists and laboratories, some conditions must be agreed at the outset. Following the Hwang scandal,[345] the importance of agreement on certain ethical issues is something that the stem cell community is particularly sensitive to. I am not suggesting that we embark on a quest to uncover a complete set of universal norms vis-à-vis bioethics, for we live in a world of many cultures, belief systems, and histories, which result in numerous and diverse perspectives of what is or is not 'ethical'. And, we need not agree on everything. However, agreement on certain ethical issues in research, such as the requirement of informed consent absent duress of the (surplus) embryo donors from which hESC lines are to be derived,[346] is necessary for international collaborations to flourish.[347]

Jasanoff, 'Judgment Under Siege: The Three-Body Problem of Expert Legitimacy' in Sabine Maasen and Peter Weingart (eds), *Democratization of Expertise?* (Springer Netherlands 2005).

[342] DeRenzo (n 340).

[343] On responsive regulation see: Ayres and Braithwaite (n 82); Nuffield Council on Bioethics, 'Public Health: Ethical Issues' (2007); Baldwin and Black (n 81). See also 5.3.1

[344] Better Regulation Task Force, 'Principles of Good Regulation' (n 14); Better Regulation Task Force, 'Better Regulation - from Design to Delivery' (n 14); OECD (n 14); 'The Five Principles of Good Regulation' (n 14); 'Better Regulation' (n 14).

[345] Susan Watts, 'South Korea's Cloning Controversy' (*BBC News - Newsnight*, 11 January 2006) <http://news.bbc.co.uk/1/hi/programmes/newsnight/4602490.stm> accessed 1 April 2015; 'South Korea to Renew Stem Cell Research after Scandal' (*BBC News - Asia-Pacific*, 19 September 2011) <http://www.bbc.co.uk/news/world-asia-pacific-14968613> accessed 1 April 2015; 'S Korea Clone Scientist Convicted' (*BBC News - Asia-Pacific*, 26 October 2009) <http://news.bbc.co.uk/1/hi/world/asia-pacific/8325377.stm> accessed 1 April 2015; Leo Kim, 'Explaining the Hwang Scandal: National Scientific Culture and Its Global Relevance' (2008) 17 Science as Culture 397.

[346] The ethical derivation of stem cell lines was one of the issues that arose in the Hwang scandal. See: Jess Buxton, 'Eggs and Ethics in Stem Cell Research' (*BioNews*, 28 November 2005) <http://www.bionews.org.uk/page_37840.asp> accessed 1 April 2015.

[347] See 1.3 and 5.2.4

The question of which ethical issues require consensus is part of a broader conversation between the various actors, groups, and institutions (see 3.4) with a stake in future of stem cell research. The substance of that conversation is outside the scope of this chapter, the purpose of which is to set up a framework that can then be used to host the conversations needed to determine which ethical issues would benefit from a universal approach, and what that approach might be. These conversations are an essential part of the proposed framework: as noted above (3.2), PBR requires an on-going 'culture' of participation, open discussion and exchange, which is critical for the success of the regime. Continued, open dialogue and debate will help ensure we reach useful, workable principles that can be amended and altered to remain relevant to states of knowledge in both science and ethics and thus facilitate progress in stem cell research.

Consensus might be desirable in relation to other elements within the research process besides the ethical norms – namely, the 'operational' issues.[348] For example, it might be helpful if laboratory standards were somewhat streamlined, or policy on classifying the derivation of stem cell lines was more clearly articulated in order to facilitate the exchange of information and import/export of cell lines and products.[349] Responses to jurisdiction-shopping for stem cell therapies and managing adverse effects thereof might benefit from agreed outcomes-orientated policy. Identifying and advancing commonality across operational issues is likely to be more easily achieved than agreement on ethical issues. That said, one must be aware of the thin line between procedural and ethical matters and take care that seemingly procedural principles do not beg moral questions under the surface. As I have already noted above (3.2.1), operational issues may seem mundane and inconsequential in comparison to the ethical questions that continue to preoccupy the field. However, the importance of good operational regulation ought not be underestimated. So much has been invested in stem cell research: time, money, and hope. Moreover, this research is being undertaken *now,* it is already in progress and unlikely to slow down. Good operational regulation will demonstrate and ensure that care is taken on matters of safety, accuracy, and record-keeping – matters that will become increasingly important as research is translated to

348 See 3.2.1

349 Geoffrey Lomax and Angela McNab, 'Harmonizing Standards and Coding for hESC Research' (2008) 2 Cell stem cell 201; Lena Eriksson and Andrew Webster, 'Standardizing the Unknown: Practicable Pluripotency as Doable Futures' (2008) 17 Science as Culture 57; Catherine Waldby and Brian Salter, 'Global Governance in Human Embryonic Stem Cell Science: Standardisation and Bioethics in Research and Patenting' (2008) 2 Studies in Ethics, Law, and Technology.

clinical therapies – thereby encouraging public confidence in science. Cross-border conversations on operational matters can build and strengthen relationships within the field; these conversations can be a stepping-stone to the trickier discussions on ethical matters. Ultimately, smooth cross-border operational regulations can expedite research itself, and the efficient realisation of research into clinical therapies. This, after all, is a primary goal of stem cell research. I return to this point to address the question of how and who might determine the said operational regulations in section 3.4.

A single body need not carry out these regulatory functions enumerated so far – there need not even be a single body performing oversight. Polycentricity encourages harnessing regulatory capacity and expertise where possible, enrolling the most appropriate actor/s for the task. This may well (in fact, is likely to) result in regulatory power being dispersed laterally rather than being held and delegated through a hierarchical structure. In the case of stem cell research, I advocate capitalizing on the concentration of international inter-disciplinary expertise housed within certain organisations.[350] Conceptualizing the regulatory field in terms of polycentricity essentially gives us a theoretical and practical framework through which such soft regulation, hitherto unrecognized, that takes place outside traditional and established governance channels, can be recognized, monitored, critiqued, and adjusted. It is true that this approach will further complicate and increase regulatory activity, and this is an important consideration. Current regulatory trends favour a 'less is more' approach, in an attempt to reduce regulatory burden.[351] However, this must be balanced against the development of a regulatory regime that is genuinely cognizant of and responsive to the complex and changing nature of stem cell research. Moreover, in light of the number of international instruments (legal and non-legal) that already govern conduct in the context of stem cell research from various angles (for example in the areas of human rights, intellectual property, commerce, employment) my suggestions are less onerous than they may initially seem.

Thus, at the international level, both polycentricism and PBR allow us to more easily acknowledge and absorb different practices across the global scientific community, and

[350] See 3.4. As noted above (n 341) considering in detail the role of expert in shaping science policy is beyond the remit of this chapter, and indeed this thesis.
[351] See for example: Hampton (n 22).
And, note the UK government's push to implement the 'one-in, two-out' policy: Department for Business Innovation & Skills (n 17) s.1.9.

to develop relationships and understanding between parties in order to better regulate. Moreover, as more flexible mode of regulation, polycentric-PBR will allow us to react speedily to developments in the field, and respond appropriately to undesirable behaviour and non-compliance if necessary.[352] These themes will be expanded upon in the following two sections.

[352] Baldwin and Black (n 81); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Ayres and Braithwaite (n 82). See 3.5

3.4 International regulatory collaborations[353]

Described as a 'patchwork'[354] or even 'patchwork of patchworks'[355] a panoramic picture of inter- and intra-jurisdictional regulation vis-à-vis stem cell research reveals its complexities: discord, fragmentation, concordance, overlaps, and gaps can all be discerned.[356] Many writers have explored the international regulatory terrain and encouraged international policy convergence.[357] Isasi and Knoppers observe that:

> '…we are witnessing a departure from an "embryo-centric" approach to one that is focused on the globalisation and governance of research and its clinical translation, along with the commercialization of future stem cell-based diagnostics and therapeutics.'[358]

Similar trends have been noted by Salter and Waldby:

> 'The development of stem cell science takes place in the context of the globalisation of all aspects of the knowledge economy of biomedicine…
>
> 'In parallel to the globalisation of the bioeconomy, a second process is also in train: the globalisation of the governance arrangements that facilitate scientific and commercial exchange.'[359]

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353 See 4.4 for a parallel argument in the context of international gene synthesis

354 Lori P Knowles, 'A Regulatory Patchwork—human ES Cell Research Oversight' (2004) 22 Nature Biotechnology 157.

355 Timothy Caulfield and others, 'The Stem Cell Research Environment: A Patchwork of Patchworks' (2009) 5 Stem Cell Reviews and Reports 82.

356 Knowles (n 354); Caulfield and others (n 355); Timothy Caulfield, Christen Rachul and Amy Zarzeczny, 'The Evolution of Policy Issues in Stem Cell Research: An International Survey' (2012) 8 Stem Cell Reviews and Reports 1037; Isasi and Knoppers, 'Mind the Gap' (n 289); Isasi (n 289); Isasi and Knoppers, 'From Banking to International Governance' (n 289); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289).

357 Caulfield and others (n 355); Caulfield, Rachul and Zarzeczny (n 356); Lomax and McNab (n 349); Isasi and Knoppers, 'Mind the Gap' (n 289); Isasi (n 289); Isasi and Knoppers, 'From Banking to International Governance' (n 289); Knoppers and Isasi (n 289); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289); P Pearl O'Rourke, Melinda Abelman and Kate Gallin Heffernan, 'Centralized Banks for Human Embryonic Stem Cells: A Worthwhile Challenge' (2008) 2 Cell Stem Cell 307; Lyn E Healy, Tenneille E Ludwig and Andre Choo, 'International Banking: Checks, Deposits, and Withdrawals' (2008) 2 Cell Stem Cell 305; Jeremy Micah Crook, Derek Hei and Glyn Stacey, 'The International Stem Cell Banking Initiative (ISCBI): Raising Standards to Bank on' (2010) 46 In Vitro Cellular & Developmental Biology-Animal 169; Rosario Isasi and Bartha M Knoppers, 'Beyond the Embryo: Transnational, Transdisciplinary and Translational Perspectives on Stem Cell Research' (2010) 7:2 SCRIPTed <http://www.law.ed.ac.uk/ahrc/script-ed/vol7-2/isasi.asp> accessed 30 March 2015.

358 Isasi (n 289); Isasi and Knoppers, 'Beyond the Embryo: Transnational, Transdisciplinary and Translational Perspectives on Stem Cell Research' (n 357).

359 Waldby and Salter (n 349); Brian Salter, 'The Global Politics of Human Embryonic Stem Cell Science' (2007) 13 Global Governance: A Review of Multilateralism and International Organizations 277; Brian Salter and Charlotte Salter, 'Bioethics and the Global Moral Economy The Cultural Politics of Human Embryonic Stem Cell Science' (2007) 32 Science, Technology & Human Values 554; Herbert Gottweis, Brian Salter and Cathy Waldby, *The The Global Politics of Human Embryonic Stem Cell Science* (First Edition, Palgrave Macmillan 2009); Catherine Waldby and Robert Mitchell, *Tissue Economies: Blood, Organs, and Cell Lines in Late Capitalism* (Duke University Press Books 2006).;

So, international convergence can occupy many dimensions: economic, political, scientific and so on. By analysing the growth of international regulatory collaborations in terms of regulatory theory within the context of polycentric-PBR this chapter intends to contribute to that body of literature, presenting a conceptual framework that may aid the future development of the said regulatory collaborations.[360]

The term 'policy interoperability'[361] referred to above is useful and to some extent captures the essence of the regulatory picture envisioned in this chapter. Interoperability is an expression of harmonization – as distinct from standardization:

> 'We see then that harmonization is a process of recognizing and reconciling differences, and hence conveys a meaning of accord or comparability between differing elements…
>
> 'Accordingly, harmonization and standardization have very distinct goals. Harmonization processes do not seek uniformity as the end result. Unification seeks standardization of policies by means of uniform model codes, guidelines or treaties which adopted and consistency applied by sovereign states.'[362]

Isasi discusses four models of interoperability:

1. Absolute ethical and legal equivalency ('unification or standardization')
2. Substantially equivalent ('high degree of similarity in core principles, but not necessary in detailed provisions')
3. Reciprocal policy agreements ('[a regulatory] entity [is] formally recognized as having adopted consistent ethical and legal requirements')
4. Emulation and transnational promotion[363]

The system of regulation advocated in this chapter can accommodate all four approaches. The analysis undertaken by Isasi and Knoppers forms an essential part of the background to this chapter as it evidences modes and instances of regulatory collaboration in the field that I view as activity characteristic of, or complementary to, either polycentricism or principles-based regulation. As such, it is a good foundation for the development of a regulatory regime envisioned in the chapter.

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[360] See chapter IV for a further example of international regulatory collaboration, in the field of gene synthesis.
[361] Isasi (n 289).
[362] Ibid 109.
[363] Ibid 112–14.

Recall that the regulatory subject matter can be broadly characterized as either operational or ethical. Operational matters such as laboratory standards are more suited to, indeed benefit from, Isasi's model 1, standardization:

> 'Standardisation is important in science because it creates the conditions for stable comparison and the interoperability of technical elements. Scientific discovery is impossible without agreed measures, protocols, classificatory systems and technical benchmarks shared by laboratories working in the same research field…'[364]

Ethical matters are much trickier; here models 2, 3 and 4 are more realistic options, and in fact are already practice.[365] One example of policy interoperability in action is the reciprocal policy agreement implemented by the California Institute for Regenerative Medicine (CIRM) that allows CIRM funding for research on hESC lines that are derived under a license issued by the UK's Human Fertilisation and Embryology Authority, or derived in accordance with the Canadian Institutes of Health Research Guidelines.[366] Furthermore, CIRM, the UK Stem Cell Bank, and the US National Academy of Sciences all utilize the 'acceptably derived' criterion for hESC lines within their policies (i.e. hESC lines derived by a specified institution are declared as acceptable – this implies acceptance of the specified institutions' ethical policy).[367] This is good starting point. But engaging in type 2, 3, or 4 convergences does not overcome the patchwork-style development of international regulation. Ideally, these instances of binary inter-jurisdictional convergence will eventually give way to multi-party international convergences (rather than a series of binary convergences), articulated through a clear framework of consensus statements and guidelines.

Yet, there will be instances where jurisdictions differ substantially on the 'core principles' or 'ethical and legal requirements'. These differences are not problematic *per se*; they will simply define the boundaries of collaboration within this particular system

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364 Waldby and Salter (n 349) 2; Stefan Timmermans and Marc Berg, *The Gold Standard: The Challenge of Evidence-Based Medicine and Standardization in Health Care* (Temple University Press 2003).
365 Isasi (n 289); Isasi and Knoppers, 'From Banking to International Governance' (n 289); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289).
366 Isasi (n 289); Lomax and McNab (n 349); Gary S Stein and others, *Human Stem Cell Technology and Biology: A Research Guide and Laboratory Manual* (John Wiley & Sons 2011); Isasi and Knoppers, 'From Banking to International Governance' (n 289); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289).
367 Lomax and McNab (n 349); Isasi (n 289); Isasi and Knoppers, 'From Banking to International Governance' (n 289); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289).

of regulation. The regulatory framework that I propose here is inspired by and based on the *voluntary* regulatory collaborations that have arisen over the past few years. So, what do these international regulatory collaborations look like? The following table (Table D) sets out key documents resulting from international collaborations that in some way purport to regulate or influence the activity of stem cell research.

TABLE D: International soft law instruments[368]

	YEAR	ORGANISATION	TITLE	CATEGORY
1	1998	International Federation of Fertility Societies (IFFS)	Human Embryonic Stem Cells and Reproductive Cloning	C
2	1999	HUGO Ethics Committee	Statement on Cloning	B
3	2000	Pontifical Academy for Life Sciences	Declaration on the production and the scientific and therapeutic use of human embryonic stem cells	C
4	2001	UNESCO International Bioethics Committee (IBC)	On the Ethical Aspects of Human Embryonic Stem Cell Research	B
5	2003	UNESCO IBC	On the Possibility of Elaborating a universal instrument on bioethics	B
6	2004	HUGO Ethics Committee	Statement on Stem Cells	B
7	2005 Amended in 2009	World Medical Association (WMA)	Statement on Genetics and Medicine (is there a 2009 version???)	B
8	2006	The Hinxton Group, an International Consortium on Stem Cells, Ethics and Law	Consensus Statement on Transnational Co-operation in Stem Cell Research	A
9	2006	International Society for Stem Cell Research (ISSCR)	Guidelines for the Conduct of Human Embryonic Stem Cell Research	A
10	2006	WMA	Statement on Assisted Reproductive Technologies	A
11	2007	ISSCR	Ethical Standards for Human to Animal Chimera Experiments in Stem Cell Research	A
12	2008	ISSCR	Guidelines for the Clinical Translation of Stem Cells	A
13	2008	ISSCR	Patient Handbook on Stem Cell Therapies	A

[368] This table was compiled using StemGen Database: 'International Database on the Legal and Socio-Ethical Aspects on StemGen Research' *(StemGen)* <http://www stemgen.org/database-laws-policies-results/International> accessed 1 April 2015. Note that there are other important international/collaborative ventures such as the UMASS International Stem Cell Bank that are not included in this table. The focus of this chapter is specifically on documents that have been produced.

14	2008	The Hinxton Group	Consensus Statement: Science, Ethics and Policy Challenges of Pluripotent Stem Cell-Derived Gametes	A
15	2009	International Federation of Gynecology and Obstetrics (FIGO)	Ethical Issues in Obstetrics and Gynecology: A Study of Ethical Aspects of Human Reproduction and Women's Health, 33-37, 47-48	C
16	2009	UNESCO IBC	On Human Cloning and International Governance	B
17	2009	WMA	Statement on Embryonic Stem Cell Research	B
18	2009	International Stem Cell Banking Initiative (ISCBI) *funded by the* International Stem Cell Forum (ISCF)	Consensus Guidance for Banking and Supply of hESC lines for Research Purposes	A
19	2009	European Human Embryonic Stem Cell Registry (EHESCR)	Code of Practice for the Operation of the EHESCR	A
20	2011	ISCF	Publishing SNP Genotypes of hESC lines: Policy Statement	A
21	2013	ISSCR	Position Statement on the Provision and Procurement of Human Eggs for Stem Cell Research	A
22	2014	EHESCR	Code of Practice for the Operation of the European Human Pluripotent Stem Cell Registry	A
23	TBA	ISCF/ISCBI	'Consensus Guidance for Banking and Supply of hESC lines for Clinical Purposes' [UNDER DEVELOPMENT]	A
24	on-going	ISSCR	Current Protocols in Stem Cell Biology	A

This is not an exhaustive list of all the regulatory collaborations on an international scale; these particular collaborations have been selected for their prominence within the field. Furthermore, not all of these collaborations are solely concerned with stem cell research, but have been included in this table to demonstrate the diverse range of international organisations that are interested in and concerned with the development of international regulation for stem cell research. Table D also shows the history of

international conversations and collaborations in the field of stem cell research and the increase in such activity in recent years. That said, given that the focus of this chapter is specifically on the regulation of stem cell research – a complex area in its own right – the organisations under the spotlight are those whose primary focus and expertise is stem cell research (The Hinxton Group, ISSCR, ISCF, EHESCR). These organisations I refer to as category A (blue). The organisations whose remit is wider but includes stem cell research, and who have specifically considered stem cell research (UNESCO IBC, WMA, HUGO Ethics Committee) I refer to as category B (purple). Finally, category C (orange) comprises those organisations whose remit does not specifically include but is relevant/related to stem cell research (IFFS, FIGO). All three categories would be included in the regulatory conversation, for each organization has a valuable perspective to share. However, for reasons of expertise, reach and efficiency, the task of regulating stem cell research will likely and logically fall to those in category A.

Examining the category A documents more closely, three distinct aims or themes emerge. Firstly, there are documents that express the relevant 'issues' in the field and guide discourse (this can be termed 'agenda-setting'). The Hinxton Group's Consensus Statement on Transnational Co-operation in Stem Cell Research is one such example. Then, there are documents that determine ethical standards and purport to guide behaviour, such as the ISSCR's Guidelines for the Conduct of Human Embryonic Stem Cell Research. Finally, there are documents that specify operational standards and procedures, such as the ISCBI's Consensus Guidance for Banking and Supply of hESC lines for Research Purposes. A single document may contain more than one aim or theme – indeed many do. For example, clauses 1-7 of the Hinxton Group's Consensus Statement on Transnational Co-operation in Stem Cell Research purport to guide current behaviour, e.g. 'Research participants and donors of human materials must provide valid informed consent, and conflicts of interest should be appropriately addressed'.[369] Clauses 16-19 on the other hand, are declared as issues due for consideration, e.g. 'However, it is imperative that international efforts to address these new issues [gametes derived from hESC, and human-non human chimeras] be initiated as soon as possible in order to ensure that science proceeds in an ethically acceptable fashion…'.[370] The ISSCR's Guidelines for the Conduct of Human Embryonic Stem

[369] The Hinxton Group, 'Consensus Statement: Transnational Co-Operation in Stem Cell Research' (2006) clause 1 <http://www.hinxtongroup.org/au_trans_cs.html> accessed 30 March 2015.
[370] Ibid clause 16.

Cell Research incorporates behavioural standards on procurement of hESC and requirement of informed consent,[371] as well as setting out at length operational guidance 'for derivation, banking, and distribution of human pluripotent stem cell lines'.[372]

These regulatory collaborations are still in their early days, and in the process of being developed and refined. Yet, within this network of organizations and matrix of documents, the beginnings of the structure and substance of an international governance scheme can be detected. These documents can be seen as articulating the principles that characterize PBR (e.g. 'Researchers must demonstrate appropriate expertise or training in the culture and maintenance of existing human embryonic stem cell lines and expertise or training in the derivation of pluripotent non-human stem cell lines before being granted permission for attempts at derivations of new human stem cell lines.'[373]) while the organizations, each with a distinct remit and expertise characterize polycentricity. However, if a polycentric PBR regime is to develop, much more needs to be done. As a first step, inter-organizational co-operation will be crucial in order to clearly delineate the purpose and scope of each organization and document so as to avoid overlaps and inconsistencies. Only then will organizations be in a position to refine and implement the regulatory principles. This is an administratively and temporally demanding task, that in order to stand a chance of success, requires the sustained commitment and initiative of all concerned organisations. It is not within my remit to set out procedures for such inter-organisational co-operation, and it is trite to reiterate that representation (of each organization), transparent conduct (e.g. keeping detailed accounts and minutes, producing regular reports etc.), consultation (within the field and the public), opportunity for open discussion and dissent, and so forth, are essential for internal and external credibility and functionality.

None of the documents from these institutions (all categories) are legally binding.[374] Indeed, a document need not be legally binding to be wide-reaching and influential:[375]

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371 International Society for Stem Cell Research, 'Guidelines for the Conduct of Human Embryonic Stem Cell Research' (2006) s.11.3 <http://www.isscr.org/docs/default-source/hesc-guidelines/isscrhescguidelines2006.pdf> accessed 30 March 2015.
372 Ibid s.12.
373 Ibid s.12.1c.
374 Having failed to pass a binding convention banning reproductive human cloning, the General Assembly of the UN issued a non-binding Declaration urging nations to ban all forms of human cloning.
375 Emily Jackson, *Medical Law: Text, Cases, and Materials* (3rd edn, Oxford University Press 2013) Chapter 9.

the WMA's Declaration of Helsinki[376] on research involving human subjects is one such example, the Nuremburg Code[377] is another, and the Council for International Organisations of Medical Sciences (CIOMS) *International Ethical Guidelines for Biomedical Research involving Human Subjects*[378] is another (in fact, all these documents are cited in the ISSCR guidelines[379]). And this is an important point. Arguably, the potential power and credibility of the organisations (category A) themselves, and by extension the documents that they publish, lies in the fact that they are self-developed, and that they are not State mandated regulatory agencies. These organisations are products of international, interdisciplinary initiatives: scientists, ethicists, and lawyers who have voluntarily taken the initiative to engage with colleagues from other countries and disciplines in the field. This demonstrates a willingness to share information and ideas, to learn, to take responsibility – qualities that are more likely to earn the respect and trust of the field and the public because they are voluntarily revealed rather than commanded. There are a number of successful, functioning non-state, transnational polycentric regimes of the type envisaged here. Social and environmental accreditation agencies such as the Fair Trade Labelling Organisation (FTLO), the Forest Stewardship Council (FSC) and the International Accounting Standards Board (IASB) are three such examples.[380] The latter is a particularly pertinent example as some of the motivations behind the development of this regime resonate with the argument put forth here:

> 'International Accounting Standards (as devised by the International Accounting Standards Board) were promulgated in order to *facilitate a convergence in national and business accounting practices and to harmonize the available information on individual business' performance.* A further aim (one driven in particular by the UK Accountancy Profession) was to avoid public (especially European Community) regulation of international accounting standards.'[381] (emphasis added)

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376 World Medical Association, 'Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964; Amended by the 64th WMA General Assembly, Fortaleza, Brazil, October 2013)' <http://www.wma.net/en/30publications/10policies/b3/> accessed 30 March 2015.

377 'The Nuremberg Code' (1949) <http://www.hhs.gov/ohrp/archive/nurcode.html> accessed 1 April 2015. [From: *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10",* Vol. 2, pp. 181-182. Washington, D.C.: U.S. Government Printing Office, 1949]

378 Council for International Organizations of Medical Sciences, 'International Ethical Guidelines for Biomedical Research Involving Human Subjects' (2002) <http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm> accessed 30 March 2015.

379 International Society for Stem Cell Research (n 371) clause 4.

380 Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332) 138. In this paper Black analyses the construction of legitimacy and accountability vis-à-vis these organisations and the regimes in which they operate; these issues will be discussed further in 3.5.1.

381 Baldwin, Cave and Lodge (n 3) 429.

At this point is useful to return to question of what regulation is *for*.[382] Simply defined, I submit that the purpose of regulation is to influence behaviour in some way, and further, that the party exerting the influence is not limited to the State or State-mandated organisations. The matter of who exerts the influence is important - a regulator with in-depth knowledge of the field of activity and access to those in the field, is more likely to understand whom and what they are regulating. This will ideally translate into more germane regulations. At this point it is important to distinguish between pure self-regulation[383] and the *knowledgeable regulator*[384] - I advocate the latter. Here, the proposed regulator is an independent, composite regulator who consists of representatives from a variety of (ideally all) actors/groups with a stake in the development and future of stem cell research. The Category A organisations referred to here are well-placed to understand what is/is not important to stem cell scientists, what sanctions and reprimands will be meaningful, what incentives and nudges[385] will be effective, and so on. Therefore, the insight that these organisations have is incredibly valuable, and properly utilized, can lend them the credibility and public confidence to lead regulation in this field.[386] That said, if these organisations are to lead the global regulation of stem cell research, it is imperative that they can demonstrate legitimacy and accountability, command compliance from the field, and enforce sanctions where necessary. It is to these issues that I now turn my attention.

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[382] On this point also see footnote 261

[383] For an overview of self-regulation, including its advantages and disadvantages please see: Baldwin, Cave and Lodge (n 3) Chapter 8; Black, 'Decentring Regulation' (n 333).

[384] Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52); Devaney, 'Regulate To Innovate' (n 52); Prosser (n 311).

[385] This refers to the regulatory trend of 'nudge governance' whereby regulators use research from the field of behavioural sciences (e.g. behaviour patterns such as cognitive biases) to steer regulatee's towards making certain choices that will ultimately lead to fulfilling a particular regulatory aim. For a full explanation and analysis of nudge governance, including in the context of healthcare see: Muireann Quigley, 'Nudging for Health: On Public Policy and Designing Choice Architecture' [2013] Medical Law Review 1; Richard H Thaler and Cass R Sunstein, *Nudge: Improving Decisions about Health, Wealth, and Happiness* (Yale University Press 2008); Cass R Sunstein and Richard H Thaler, 'Libertarian Paternalism Is Not an Oxymoron' [2003] The University of Chicago Law Review 1159; Richard Thaler, Cass Sunstein and John Balz, 'Choice Architecture' [2010] SSRN <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1583509> accessed 1 April 2015.

[386] For a further example of a potential 'knowledgeable regulator' in the field of emerging biotechnologies see chapter IV; I advance a similar argument in the context of international gene synthesis.

3.5 Challenges to consider

No regulatory approach is perfect, and polycentric PBR is no exception. There are numerous theoretical as well as practical challenges to this approach; some have been much discussed and debated,[387] others may become apparent as these approaches settle and mature. Despite contributing significantly to the development of PBR and decentred regulatory structures Black has also been one of its shrewdest critics.[388] In a recent paper reflecting on the short histories of four NG techniques in the context of financial services regulation, including PBR, she writes of the need to better understand the multiple and complex dimensions (organizational, functional, and cognitive) of these techniques - the tensions, ambiguities, vulnerabilities, paradoxes and contradictions - in order to better understand their operation and character.[389] Critical to the ambition of responsive and responsible regulation is the recognition that 'things will always go wrong', [390] not just for reasons listed above, but also because of unintended consequences and side effects as well as plain regulatory failure.[391] Yet, it is my contention that the scheme proposed here is the one that is best suited to stem cell research for the reasons recounted throughout this chapter. Regulators in the stem cell field can certainly learn from the experiences of NG the financial sector:

> 'If the financial crisis has a broader lesson for regulators elsewhere it is this: it is not enough to ask regulators or others to engage in self-critical learning, to assess whether they are performing their tasks well. It has to be asked whether they are performing the right tasks at all…'[392]

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387 Steven L Schwarcz, 'The "Principles" Paradox' (2009) 10 European Business Organization Law Review 175; Marianne Ojo, 'Building on the Trust of Management: Overcoming the Paradoxes of Principles Based Regulation' <http://mpra.ub.uni-muenchen.de/22500/> accessed 30 March 2015; Ford, 'New Governance in the Teeth of Human Frailty' (n 262); Ford, 'Principles-Based Securities Regulation in the Wake of the Global Financial Crisis' (n 292); Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40); Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332).

388 Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332); Black, Hopper and Band (n 40); Black, 'Paradoxes and Failures' (n 40); Black, 'Decentring Regulation' (n 333).

389 Black, 'Paradoxes and Failures' (n 40) 1056–7. See 4.5 for a parallel analysis on risk-based regulation (in the context of international DNA synthesis).

390 Ibid 1063.

391 Black, 'Paradoxes and Failures' (n 40).

392 Ibid 1062.

So, reflexivity is key although this is easier said than done. Ultimately the failure or success of regulation will be dependent on the behaviour of those participating in the regime; regulatory tools (NG or otherwise) alone cannot guarantee good regulation.[393]

These experiences need not discourage efforts to implement NG techniques in the field of stem cell research. Certainly, there are valuable lessons to be learned, but we must also bear in mind that stem cell research is a very different field to the financial services sector, despite similarities in pace (both are fast-moving fields) and complexity. It is comprised of different participants, with different goals, and of course will be faced with different challenges. Here, I discuss some of the practical challenges to the proposed system of regulation; both pertain to matters of oversight. The first issue is split into three: legitimacy, accountability and enforcement. The second issue is that of extra-territorial criminal liability vis-à-vis cross-border stem cell research collaborations.

3.5.1 Legitimacy, accountability, and enforcement[394]

Both polycentricism and PBR are vulnerable to critique when it comes to issues of legitimacy, accountability and enforcement.[395] However, as noted above every regulatory approach has its vulnerabilities to overcome, and it is as much the actors and their attitudes within the regime that determines its success or failure, as it is the chosen approach in itself. I submit that the approach advocated here is not only a good regulatory fit in theoretical terms, but also that by employing thought and care in the development and implementation process, many pitfalls (both theoretical, and as experienced by other, similar regimes) may be avoided. The discussion that follows demonstrates how challenges pertaining to legitimacy, accountability and enforcement in the proposed regime might be overcome.[396]

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393 Ford, 'New Governance in the Teeth of Human Frailty' (n 262); Black, 'Paradoxes and Failures' (n 40) 1062.

394 See 4.5.4 for a parallel argument on matters of legitimacy, accountability and enforcement in the context of international gene synthesis regulation, and also 5.3.1

395 Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40); Colin Scott, 'Accountability in the Regulatory State' (2000) 27 Journal of law and society 38; Ford, 'Principles-Based Securities Regulation in the Wake of the Global Financial Crisis' (n 292); Ford, 'New Governance in the Teeth of Human Frailty' (n 262); Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Scott, 'Regulation in the Age of Governance' (n 9).

396 I am not alone in this optimistic outlook. See: Caulfield and others (n 355); Caulfield, Rachul and Zarzeczny (n 356); Lomax and McNab (n 349); Isasi and Knoppers, 'Mind the Gap' (n 289); Isasi (n 289); Isasi and Knoppers, 'From Banking to International Governance' (n 289); Knoppers and Isasi (n 289); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289); O'Rourke, Abelman and Heffernan (n 357); Healy, Ludwig and Choo (n 357); Crook, Hei and Stacey (n 357); Isasi and Knoppers,

Decentred and alternative structures of regulation challenge traditional tests and markers of regulatory legitimacy and accountability.[397] The task that these regimes face in proving possession of these essential qualities is therefore a significantly tougher, although not impossible, one.[398] It is important to bear in mind that the challenging characteristics (e.g. a lack of central authority, international context, and hybrid structure) are the hallmarks, indeed advantages, of this style of regulation. How then, do regulators respond to demands to show legitimacy and accountability? Julia Black has suggested that we need to gain a deeper understanding of these challenges by analysing the construction and contestation of legitimacy and accountability within the relational dynamic of regulator and regulatee, before considering any further proposals on how to enhance these qualities.[399] She focuses on:

> '…the role of the institutional environment in the construction of legitimacy; the dialectical nature of accountability relationships; and the communicative structures through which accountability occurs and legitimacy is constructed.'[400]

And:

> '…how organizations in regulatory regimes respond, or are likely to respond, to multiple and often conflicting legitimacy and accountability claims, and how they themselves seek to build legitimacy in complex and dynamic situations.'[401]

Underlying these inquiries is the question of what it means to be legitimate (in the procedural or normative sense[402]) and accountable. Black's analysis shows that the question will not return a single or simple answer, for legitimacy and accountability will mean different things to different people – including the regulator.[403] These are important inquiries. However, the regime proposed here is, at best, nascent rendering it

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'Beyond the Embryo: Transnational, Transdisciplinary and Translational Perspectives on Stem Cell Research' (n 357). And see 4.5.4, 5.4.1 too on these matters.

397 Baldwin, Cave and Lodge (n 3) 25–38, 338–55, 437–8.

398 Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332).

399 Ibid.

400 Ibid 139.

401 Ibid.

402 Devaney describes legitimacy as two-fold: procedural and normative, corresponding to a regulator's executive and advisory roles (Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52) Chapter 3.) Black subdivides 'legitimacy' further into in the constitutional, justice, functional, or democratic claims (Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332).)

403 Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332).

impossible to examine the specific relational dynamics at play in a practically meaningful way, and a theoretical or speculative discussion is outside the constraints of this thesis. Suffice it to say that in the context of stem cell research, the regime proposed here will face administrative burdens of demonstrating procedural legitimacy like any other. On the other hand, normative legitimacy (particularly, if a regulator were to move beyond the operational sphere) will prove more challenging given the philosophically controversial nature of stem cell research.[404] Yet this would not be impossible – extensive consultation, debate, and deliberation behind each *reasoned* decision, can help bestow and maintain normative legitimacy upon a regulator. Nevertheless, the fact remains that the regulators will be called upon to demonstrate legitimacy and accountability, and without the support of political processes or legal authority, non-state actors, such as Category A organisations, face a tougher challenge.[405]

In response to this challenge, there are a number of traditional mechanisms that actors called upon to demonstrate legitimacy and accountability in polycentric, international regimes can exercise. These include establishing transparency and fairness through: clearly articulating objectives, strategies and procedures; consulting; conducting and publishing reviews and reports on progress; ensuring procedural fairness; giving reasons for decisions; information disclosure; implementing a complaints/appeals procedure; encouraging participation; gathering and acting on feedback; demonstrating efficacy and so forth. Rigorously pursuing these mechanisms can bestow and evidence qualities of legitimacy and accountability. Furthermore, it is important to remember that the political electoral process is not the only way of establishing legitimacy and holding regulators to account. Social and economic pressure, such as lobbying and boycotting, can be highly persuasive.[406]

There are other mechanisms of establishing legitimacy and accountability that are more 'natural' to the proposed regime. A critical quality of the regime that I propose here is

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[404] Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52) Chapter 3.
[405] Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332).
[406] One example of this is the development of the Kimberley process: Baldwin, Cave and Lodge (n 3) 430; Christine Jojarth, *Crime, War, and Global Trafficking: Designing International Cooperation* (Cambridge University Press 2009). Although note that the regime's effectiveness has subsequently been questioned: James Melik, 'Diamonds: Does the Kimberley Process Work?' (*BBC News - Business*, 28 June 2010) <http://www.bbc.co.uk/news/10307046> accessed 1 April 2015. See also: 4.5.4, 5.3.6, 5.4.1

its *voluntary* nature.[407] The number of interdisciplinary, international initiatives that have arisen over the past two decades reveal two important points about the stem cell research community: firstly, a demand for international regulation from *within* the research community and secondly, actual engagement with the task of regulating. The international organisations and the resulting documents discussed above are self-developed efforts to address the challenges of cross-border research. Whatever the complexities of the regulator-regulatee dynamic in various national settings, at the international level, it is the field – those in the traditional 'regulatee' role – that is proactively seeking regulatory progression.[408]

This level of participation from the 'regulatee' perspective is valuable: those undertaking work in this highly specialized, skilled field know the realities and limits of their work, and have experience in the practical challenges of international collaborations. However, the participation of multiple parties from alternate perspectives (governments, inter-governmental organisations, NGO's, INGO's, industry, businesses, interest groups, research institutes and so on) is also valuable, not only in the interests of developing a more nuanced, perceptive regime, but because it can be exploited as an alternative mechanism of accountability.

Firstly, it ensures questioning and cross-examination from numerous standpoints, simultaneously. In other words, tension, conflict and competition between parties can be exploited to hold one another to account.[409] Thus, the international and interdisciplinary elements of these regulatory collaborations build a subtle internal system of 'checks and balances' through diverse and concurrent channels of accountability.[410] This can also mitigate regulatory capture[411] by a particular section of the stem cell field or industry. International, polycentric regimes may be contested on grounds of private sector, or non-governmental, involvement.[412] This contestability too can be exploited as a method of on-going critique and accountability.[413] Secondly, the range of perspectives will prompt continuous discussion and debate – *communication* –

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[407] See also chapter IV
[408] This is also true for other fields within the broad area emerging biotechnologies; for example international gene synthesis (chapter IV, particularly 4.4)
[409] Scott, 'Accountability in the Regulatory State' (n 395). See also 5.4.1
[410] Ibid.
[411] Baldwin, Cave and Lodge (n 3) 43–5.
[412] Ibid 427.
[413] Ibid 438.

and develop relationships between a diverse array of actors. This in turn can encourage a more consultative and deliberative-learning style of regulation that also serves as an alternate channel of accountability.[414] Furthermore, the structure of decentred regulation promotes openness, allowing a wider range of actors to participate and hold the regime to account.

This is a good starting point for the development of stable, well-informed and facilitative international regulation. It is anticipated that through the process of regulatory development - the development of agreed operational and ethical standards - the reputation of the regime will also develop and strengthen encouraging continuous participation from the research community.

An important aspect of establishing legitimacy is demonstrating efficacy – particularly through compliance and enforcement (this is a circular point, as equally importantly, legitimacy will encourage compliance). Ensuring compliance need not be any more arduous policing task in this regime than any other. After all, these regulations are not compelled, but self-developed. There is little incentive to breach self-imposed regulatory standards, and too much to lose: reputation, trust, and relationships. These are intangible, but highly valuable assets. A regulatory breach would negatively affect all three interlinked assets for the party in breach, both internally (within the regulatory regime) and externally (those outside the regime).[415] Additionally, in practical terms substandard or 'unethical' science has poor returns, stifling opportunities for publication, funding, promotion and recognition that are essential to personal and institutional success. The reputation of the regime itself, as well as the trust and relationship between the regulatory regime and civic society, would be tarnished as well, inviting the imposition of traditional, hard law measures of the strictest kind as a reaction to the 'failure' of soft(er)/semi-self regulation.

Two further points are important to the way in which regulators respond to non-compliance or threats of non-compliance in the regime proposed here. Firstly, as noted in section 3.2, successful PBR relies on continuing dialogue and the development of relationships between parties in the regime. This is crucial, not just for the interpretation and application of principles, but also in the enforcement of principles

[414] Ibid 350, 438. See 5.4.1
[415] On this point see 4.5.4, 5.4.1

and sanctions when necessary.[416] Unlike a rules-based regime, compliance here means complying with the *spirit* of the principle. Under PBR this is ideally an iterative, learning-process between regulator and regulatee; the regulatee can clarify the purpose of the principle and how to achieve compliance, and the regulator has the flexibility and opportunity to understand the reasoning behind regulatees' actions, then assess compliance contextually and within the spirit of the principle.[417] In a Utopic PBR regime, enforcement is achieved in a non-aggressive, sensitive manner.[418] This process has the advantage of allowing regulators to gain insight into their regulatees' motivations (and vice versa), which hopefully equips them with the understanding to develop the regime in a more meaningful way.

Secondly, and following on from the first point, PBR gives regulators the flexibility to regulate *responsively*.[419] This refers to Ayres and Braithwaite's enforcement pyramid comprising a range of enforcement methods: regulatory intervention begins at the lowest level (the bottom of the pyramid) and escalates thenceforth to the highest level of intervention (apex of the pyramid).[420] As already noted, the inclusion of Category A organisations in particular, provides the regime with a route to understanding the various tensions and motivations at play within the field of stem cell research. This will enable them, as key (potential) regulators, to design meaningful and realistic obligations and sanctions. Adopting this 'tit-for-tat' approach to enforcement further maximizes these organisations' ability to exercise their insight and knowledge of the field to apply contextually and culturally meaningful sanctions that will resonate with the non-compliant party, the research community, and wider public.[421] Given this is a soft law regime the gradient of the pyramid will not be *as* steep (there is no recourse to the civil or criminal legal sanctions – unless, of course, over time the regulatory regime is incorporated into the legal regime[422]), however there is still scope within softer regimes

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416 Black, Hopper and Band (n 40) 195.
417 Ibid.
418 Black, Hopper and Band (n 40). See the same article for an analysis of the challenges and pitfalls of PBR.
419 Ayres and Braithwaite (n 82); Baldwin and Black (n 81). See 4.5.4 for a parallel argument in favour of *really responsive* risk-based regulation in the international DNA synthesis industry.
See also: Vibeke Lehmann Nielsen and Christine Parker, 'Testing Responsive Regulation in Regulatory Enforcement' (2009) 3 Regulation & Governance 376; Christine Parker, 'The "Compliance" Trap: The Moral Message in Responsive Regulatory Enforcement' (2006) 40 Law & Society Review 591.
420 Ayres and Braithwaite (n 82).
421 Ibid; Baldwin and Black (n 81).
422 For example, the European Union has incorporated the IASB's International Accounting Standards into their legal framework (Baldwin, Cave and Lodge (n 3) 429.). Note that there is another way in which a (semi)-self regulatory regime can derive legitimacy, namely, by 'borrowing' it from the State (Black,

to escalate the mode of enforcement, e.g. from persuasion (at the base of the pyramid) to loss of access to data and cell lines or loss of cell line depository rights (mid-pyramid) to exclusion from the regime/community and loss of accreditation (at the peak of the pyramid).

Ultimately, it is imperative that compliance is monitored, and regulations and sanctions enforced consistently by the various operators throughout the regime - in other words, regulators must actually engage in regulating! This is particularly important as stem cell research develops from theory to applicable clinical therapy.[423] What becomes evident from the foregoing discussion is that in order to attain a convincing regulatory regime, a nexus between understanding the intricacies and challenges of both the field of stem cell research and the chosen regulatory method(s) is crucial – thus, emphasizing the importance of a knowledgeable regulator.[424]

3.5.2 Compelling regulatory compliance: the UK Stem Cell Bank example

So, we have seen above there are rational incentives for regulatory compliance that do not include the avoidance of sanctions. Even so, the enforcement of a particular set of standards can be compelled through the structure and operation of a particular system. The UK Stem Cell Bank (UKSCB) is a good example of this form of operational standard setting. The UKSCB allows researchers from anywhere in the world to deposit and access stem cell lines provided they meet the standards prescribed in the Code of Practice.[425] Applications to deposit or access stem cell lines are made to the Steering Committee for the UK Stem Cell Bank and for the Use of Stem Cell Lines who consider each application on a case-by-case basis. So, for example, in order to deposit stem cell lines with the UKSCB the UK Steering Committee must be satisfied that the stem cell lines 'have been ethically sourced, with fully informed donor consent, and that the cell lines present a valuable resource for the biomedical research community.'[426] In

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'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332) 148.).

[423] This is beginning to take place. See for example: Panizzo (n 259); Hyder, 'Stem Cell Therapy for Autism Gets Clinical Trial Go-Ahead' (n 259); Retassie (n 259); Paxman (n 259); Hyder, 'Italian Government Orders Trial of Controversial Stem Cell Therapy' (n 259); Harwood (n 259); Aitsi-Selmi (n 259); Young (n 259); Baker (n 259); Ilic (n 259); Steer (n 259); Tierney (n 259).

[424] Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52) Chapter 3.

[425] UK Stem Cell Bank, *Code of Practice for the Use of Human Stem Cell Lines* (2010) <http://www.mrc.ac.uk/documents/pdf/code-of-practice-for-the-use-of-human-stem-cell-lines/> accessed 30 March 2015.

[426] Ibid 6.1.

order to access a hESC lines from the UKSCB the UK Steering Committee must be satisfied that the hESC lines

> '…are only used by bona fide research groups for justified and valuable purposes that reflect the requirements of the law relating to this area. This is:
>
> a) research which increases the knowledge about the development of embryos or has the long term goal of helping to increase knowledge about serious diseases and their treatment (as set out in the 1990 Act as amended by the 2008 HFE Bill);
> b) basic cell research which underpins these aims (as recommended in the House of Lords Report 2002);
> c) development of cell based therapies for clinical trials in respect of serious human diseases.'[427]

Applicants must submit an application form together with any requested documents, in order for the UK Steering Committee to consider their request and determine a result.

The UKSCB is considered successful due to its clear, transparent, and comprehensive governance policy and operational infrastructure.[428] It can guarantee products that meet certain standards establishing its reputation as a valuable international resource. As the process of working with the UKSCB necessitates compliance with the Code of Practice (for UK based and international researchers), the UKSCB effectively disseminates its own standards and controls internationally:

> 'So in this way the UKSCB has positioned itself as a key broker and negotiator across the transnational networks of the international scientific community. As the global leader in brokering technical standardisation, and as the access point to well characterised and stabilised stem cell stock, it is a key creator and enforcer of the material standards which will mediate relationships between key laboratories in the field.'[429]

Again, this manner of standard setting is based on voluntariness, for an institution might just as easily opt not to work with the UKSCB. However, working with the UKSCB has advantages (the guarantee of certain ethical and operational standards, for instance) and this provides incentive to use the UKSCB resource. This is key for the success of such a model (UK based or international) and rests on two interlinked conditions: the

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[427] Ibid 7.1.
[428] O'Rourke, Abelman and Heffernan (n 357); Isasi and Knoppers, 'Governing Stem Cell Banks and Registries' (n 289).
[429] Waldby and Salter (n 349); Waldby and Mitchell (n 359).

reputation of the governing body (e.g. UKSCB and the UK Steering Committee), and ensuring that the advantages of working within the regime outweigh the alternatives. This model is an example of a simple yet effective method of 'international' regulation. Of course, for it to operate smoothly as an acknowledged international regime would require altering the 'UK-specific' composition of the operation to an international composition.

The foundational stages of such a scheme are already underway. Led by the UKSCB, International Stem Cell Banking Initiative (ISCBI) was formed in 2008, which:

> '…aims to create a global network of stem cell banks …share knowledge about ethical and regulatory issues in member countries and assist in the development of an agreed set of international standards for banking, characterisation and testing, thereby creating a solid ethical framework for international stem cell banking and research.'[430]

ISCBI is seen as the 'forerunner to a stem cell banking network' charged with the task of 'creating the foundations of human stem cell banking as a global enterprise'.[431] To date, ISCBI's main output has been the development of a Registry, and the publication of 'Consensus Guidance for Banking and Supply of hESC lines for Research Purposes' (guidance for clinical grade stem cell lines is currently under development). This is a promising start. However further efforts are required in order transpose the strong schemata and reputation of the UKSCB into an acceptable, functional international regime.

3.5.3 Extra-territorial criminal liability

Regulation has at its disposal many tools, including the force and span of the criminal law. Here, I have argued in favour of combining hard law and soft law in order to regulate appropriately and holistically. However, occasionally the tension between particular hard and soft regimes, between particular CAC and NG approaches comes to the fore;[432] the extra-territorial criminalization of certain research practices used in the field of stem cell research is one example.

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[430] 'International Stem Cell Banking Initiative' (*International Stem Cell Forum*) <http://www.stem-cell-forum.net/initiatives/international-stem-cell-banking-initiative/> accessed 1 April 2015.
[431] Crook, Hei and Stacey (n 357).
[432] See 5.3

The derivation of stem cell lines from a human embryo is a practice that is contested on ethical grounds (specifically, the moral status of the embryo) and in Ireland, France, Germany, Austria and Italy this practice is prohibited.[433] If a country chooses to criminalize certain stem cell research practices *within* its sovereign territory, that is of course their prerogative. This does not pose an insuperable problem for the regulatory framework that I propose here; it simply limits its reach. In countries enforcing a territorial prohibition on the derivation of hESC, scientists wishing to use this technique would be free to leave their home country and take up a position in another country, where the practice is legal. In doing so, they might be including themselves in the international regulatory regime proposed here, depending on the host country or institution.

However, when countries impose extra-territorial liability on scientists, international scientific and regulatory collaborations can suffer. This is not an abstract juridical issue. German law was thought to have extra-territorial effect, restricting German scientists' capacity to (legally) derive hESC lines and carry out research on new hESC lines.[434] This was a widely held view amongst both the research and legal community.[435] In August 2008 this was clarified and reported:

> '…the members of the Bundestag have also specified the scope of application of the Stem Cell Act: as it explicitly refers to the utilization of human embryonic stem cells in Germany, the work of German scientists abroad (e.g. in the context of international projects) will no longer constitute a criminal offence.'[436]

Although this particular instance of extra-territorial liability has been resolved for German researchers in the field, the same tensions might easily arise in the context of another technique, or vis-à-vis another country. In short, the issue persists.

The issue of extra-territorial liability has been specifically acknowledged by the Hinxton Group; the opening paragraphs of Consensus Statement on Transnational Co-operation in Stem Cell Research (2006) states:

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433 Knowles (n 354).
434 Gretchen Vogel, 'Visiting German Profs Could Face Jail' (2003) 301 Science 577.
435 Benjamin J Capps and Alastair V Campbell, *Contested Cells: Global Perspectives on the Stem Cell Debate* (World Scientific 2010).
436 Ira Herrmann, Christiane Woopen and Oliver Brustle, 'German Parliament Passes Amendment to Stem Cell Act' (*EuroStemCell*, 26 June 2008) <http://www.eurostemcell.org/commentanalysis/german-parliament-passes-amendment-stem-cell-act> accessed 1 April 2015.

> 'Inconsistent and conflicting laws prevent some scientists from engaging in this [hESC] research and hinder global collaboration. Societies have the authority to regulate science, and scientists have a responsibility to obey the law. However, policy makers should refrain from interfering with the freedom of citizens unless good and sufficient justification can be produced for doing so.'[437]

Principles 4 and 5 of the same Consensus Statement read:

> 4. In countries with laws that restrict elements of human embryonic stem cell (hESC) research but that do not expressly prohibit international collaborations, research institutions should neither discriminate against nor restrict the freedom of their investigators who want to travel to do work that is undertaken with scientific and ethical integrity.
>
> 5. Law makers should be similarly circumspect in restricting citizens' conduct extraterritorially with regard to stem cell research. So long as scientifically and ethically defensible hESC research is undertaken in a country in which it is legally permissible, scientists should be free to participate in that research without fear of being liable to prosecution, restriction, or discrimination in another jurisdiction.[438]

Extra-territorial liability creates barriers that are significantly more difficult to surmount, restricting international collaborations from the perspective of both science and regulation. The question of whether this domain is/ought to be subject to extra-territorial laws has been much confronted in legal and ethical discourse.[439]

This thesis is not the forum to discuss the underlying jurisprudential questions of legitimacy *a propos* extra-territoriality. Nor will I delve into philosophical debates on the ethics of imposing extra-territorial liability for elements of stem cell research.[440] However, it is important to recognize the existence of tensions between the freedom to pursue (ethically defensible) scientific research, and the sovereign right of states to exert extra-territorial powers.[441] For, these tensions will continue to impede international

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[437] The Hinxton Group (n 369).
[438] Ibid Principles 4, 5.
[439] Loane Skene, 'Undertaking Research in Other Countries: National Ethico-Legal Barometers and International Ethical Consensus Statements' (2007) 4 PLoS medicine e10; Heidi Mertes and Guido Pennings, 'Cross-Border Research on Human Embryonic Stem Cells: Legal and Ethical Considerations' (2009) 5 Stem Cell Reviews and Reports 10; Capps and Campbell (n 435); Debra JH Mathews and others, 'Integrity in International Stem Cell Research Collaborations' (2006) 313 Science 921.
[440] Mertes and Pennings (n 439).
[441] Skene (n 439); Mertes and Pennings (n 439); Capps and Campbell (n 435).

collaborations and the development of a cohesive international community, until an agreement – or compromise – is reached.

3.6 Conclusion

International research and regulatory collaborations in the field of stem cell research have stimulated discussions as to the necessity and development of a formalized regulatory framework in this area. I have argued here that given the complex, fast-paced nature of stem cell research itself, and the structural and relational dynamics already at play in the international arena, a framework based on polycentric PBR is apposite. Polycentric PBR is an adaptable, *sustainable* form of regulation: principles afford flexibility to keep a-pace with scientific and social changes, and can facilitate innovation; polycentricism disperses the task of regulation to the appropriate organization(s) within the network. Moreover, the process of developing, interpreting, applying and enforcing useable principles encourages dialogue and relationship-building between the many parties holding a stake in the regulation of stem cell research – this, in itself, is desirable. This regulatory approach provides a medium through which commonality can be ascertained and organized, and differences (inescapable in the field of stem cell research) recognized and absorbed. Thus, policy interoperability, rather than policy uniformity is advocated. Regulatory competition can be healthy; in the international arena, compatibility rather than conformity is required.

I have argued that a polycentric PBR regime is already in the process of organic development as evidenced by the growing number of international regulatory collaborations offering guidance and instruction to practitioners in the field. Of the numerous organizations producing guidance relevant to the conduct of (cross-border) stem cell research, a handful – Category A – have emerged as possessing the knowledge and capacity to become key regulators in an international regime. It is hoped that conceptualizing these regulatory collaborations in the terms of polycentric PBR will provide a useful theoretical framework through which the regime may be developed and strengthened, and the challenges anticipated and confronted, in the quest to harness the potential of stem cells.

CHAPTER IV

Regulating risk in synthetic biology: constructing international standards and practices for DNA design

4.1 Introduction

Imagine a world where pumpkins grow into designer houses,[442] where gardens are illuminated by trees emitting a soft golden light,[443] and flowers sing and sway in harmony.[444] It may seem like the work of a well-funded, Hollywood special cinematic effects team, but in fact, scientists in the emerging field of synthetic biology are working to make these imaginings reality.

So, what exactly is synthetic biology? Defining synthetic biology precisely is difficult[445] for it is a field that is still developing and finding the parameters of its disciplinary reach.[446] Synthetic biology is a multidisciplinary field, 'inspired by the convergence of nanoscale biology, computing and engineering'.[447] It refers to both:

a) the design and fabrication of biological components and systems that do not already exist in the natural world; and
b) the re-design and fabrication of existing biological systems[448]

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442 Steward Brand, 'Drew Endy, Jim Thomas: Synthetic Biology Debate' (*The Long Now Foundation*, 17 November 2008) <http://longnow.org/seminars/02008/nov/17/synthetic-biology-debate/> accessed 1 April 2015.
443 Timon Singh, 'Gold Nanoparticles Could Transform Trees Into Street Lights' (*inhabitat*, 30 November 2010) <http://inhabitat.com/gold-nanoparticles-could-transform-trees-into-street-lights/> accessed 1 April 2015; 'Glowing Plant: Natural Lighting without Electricity' (*Glowing Plant*) <http://www.glowingplant.com/> accessed 1 April 2015.
444 David Benque, 'Acoustic Botany' (*David Benque*, 23 June 2010) <http://www.davidbenque.com/projects/acoustic-botany> accessed 1 April 2015.
445 Jim Thomas, 'What-Syn-a-Name?' (*The Guardian: Political Science blog*, 8 July 2014) <http://www.theguardian.com/science/political-science/2014/jul/08/what-syn-a-name> accessed 1 April 2015; Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks and Scientific Committee on Consumer Safety, 'Opinion on Synthetic Biology I: Definition' (2014) <http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_044.pdf> accessed 31 March 2015.
446 Editorial, 'Tribal Gathering' (2014) 509 Nature 133; 'Synthetic Biology: Beyond Divisions' (2014) 509 Nature News 151; James J Collins and others, 'Synthetic Biology: How Best to Build a Cell' (2014) 509 Nature 155.
447 ETC Group, 'Extreme Genetic Engineering: An Introduction to Synthetic Biology' (2007) 1 <http://www.etcgroup.org/sites/www.etcgroup.org/files/publication/602/01/synbioreportweb.pdf> accessed 31 March 2015.
448 'Synthetic Biology: FAQ' (*syntheticbiology.org*) <http://syntheticbiology.org/FAQ.html> accessed 1 April 2015.

Thus, the emergence of synthetic biology requires further classification of living organisms in order to delineate the naturally occurring from the man-made. This field holds the potential to radically alter our experience and understanding of the world in which we live (see below for examples);[449] how soon and to what extent it does so is yet to be ascertained. One factor that will determine this is regulation: if we elect to target regulation specifically for synthetic biology – and there are good reasons as to why we should – what style of regulation should we opt for, which activities should we target and who should play the role of regulator? These questions are the focus of this chapter. As the field of synthetic biology is beginning to display real-world applications of the science, it is timely to consider matters of regulation.

This chapter specifically considers the regulation of one area of synthetic biology that is showing particular promise and popularity, namely, gene or DNA synthesis (see 4.2.1). To date, there are no 'hard laws' targeting DNA synthesis, or any other area of synthetic biology. Formal regulatory frameworks developed to tackle genetic modification and recombinant DNA are said to embrace their trendy descendant, synthetic biology.[450] Yet, as demonstrated by the recent Glowing Plants Project controversy (see 4.3.2) whether they in fact do so can depend on semantics, resulting in products of synthetic biology (in this case, specifically, gene synthesis) potentially being released into the environment without prior scrutiny and outside an appropriate framework for on-going oversight. As demonstrated in the discussion of benefits/risks below, the effects of unchecked product release might pose serious threats.

In the absence of formal regulation the international gene synthesis community has collaborated to develop two competing protocols that aim to prevent potentially dangerous material produced and sold by gene synthesis companies from falling into the wrong hands.[451] Here, I argue that these soft law initiatives, produced and implemented

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[449] Patrick Heavey, 'Ethical Issues in Synthetic Biology' (The University of Manchester 2012) 17 <https://www.escholar.manchester.ac.uk/api/datastream?publicationPid=uk-ac-man-scw:196435&datastreamId=FULL-TEXT.PDF> accessed 1 April 2015.

[450] See 2.3

[451] IASB, *The IASB Code of Conduct for Best Practices in Gene Synthesis* (2009) <http://www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_code_of_conduct_final.pdf> accessed 31 March 2015; IGSC, *International Gene Synthesis Consortium (IGSC) Harmonized Screening Protocol* (2009) <http://www.genesynthesisconsortium.org/images/pdf/IGSC%20Harmonized%20Screening%20Protocol-11_18_09.pdf> accessed 31 March 2015.

by those who would traditionally be designated 'regulatees', are apposite for a number of reasons.[452]

Foremost, I advocate adopting Black and Baldwin's theory of 'risk-based regulation'[453] (RBR) as part of regulatory and policy approach for DNA synthesis. Responding to the dual-use dilemma (see below) exemplified in the area of gene synthesis, and the practice of the technique by a dispersed population, I argue that RBR will enable early-stage research to continue and the biotech industry to grow by focussing regulatory resources on targeting, containing and minimizing high-priority risks. I argue that this approach is in fact exemplified in the industry-led regulatory initiatives, for, viewed through the lens of regulatory theory, these initiatives can be conceptualized in terms of RBR. Furthermore, I argue that the dissolution of the traditional regulator-regulatee distinction in this instance is advantageous; as regulatees stepping into the regulator role, the two competing organisations are armed with the technical and strategic insider knowledge to guide effective regulation.[454]

Importantly, the focus of this chapter is the dimension of international governance, for synthetic biology operates in the international context.[455] Research across this field is shared in international, peer-reviewed journals, and there are examples of international collaborations in research.[456] The BioBricks Foundation[457] hosts an international competition (iGEM)[458] and international meetings on synthetic biology to share and

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[452] This argument runs in parallel to the one put forward in chapter III in the context of international stem cell research. See particularly: 3.4

[453] Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57); Black, 'Risk-Based Regulation: Choices, Practices and Lessons Being Learned' (n 57); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Black, 'The Role of Risk in Regulatory Processes' (n 57); Baldwin, Cave and Lodge (n 3); Black and Baldwin, 'When Risk-Based Regulation Aims Low' (n 57).

[454] Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52).

[455] For a parallel argument on the governance of international stem cell research see chapter III, particularly 3.4

[456] See for example: N Annaluru and others, 'Total Synthesis of a Functional Designer Eukaryotic Chromosome' (2014) 344 Science 55; Elizabeth Pennisi, 'Building the Ultimate Yeast Genome' (2014) 343 Science 1426; Rhys Baker, 'Synthetic Biology Moves beyond Bacteria and Viruses with "Man-Made" Yeast Chromosome' (*BioNews*, 31 March 2014) <http://www.bionews.org.uk/page_408924.asp> accessed 30 July 2014.

[457] 'BioBricks Foundation: Biotechnology in the Public Interest' (*BioBricks Foundation*) <http://biobricks.org/> accessed 1 April 2015.

[458] 'Synthetic Biology Based on Standard Parts' (*iGEM*) <http://igem.org/Main_Page> accessed 4 August 2014.

develop knowledge within a community.[459] The DIY biology community disseminates and discusses their work on the worldwide web[460] – an international platform. And, most importantly, for the purposes of this chapter, commercial gene synthesis companies operate internationally. So, a researcher in California might be working with genes that s/he ordered and received from a company based in China.[461] Given this, it makes sense to consider regulation in this field from an international perspective. Moreover:

> 'International regulation has greater potential than regulation at other levels to contribute to a more even distribution of benefits and to establish measures to ameliorate negative impacts. It can play a role in introducing accountability and responsibility for management of transnational risks; help to balance the varying needs and interests of different countries; and promote transfer of technology, financial assistance, information and skills for capacity building.'[462]

Crucially, the European Group on Ethics in Science and Technology[463] and the President's Commission on Bioethics[464] have acknowledged the need for a collective international approach to the governance of synthetic biology.[465]

Before proceeding to the detail of these arguments, it is important to step back and consider why targeted regulation is necessary in this area. To do so, requires some

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459 The most recent meeting was held in July, 2013 in London: 'SB6.0: The Sixth International Meeting on Synthetic Biology' (*BioBricks Foundation*) <http://sb6.biobricks.org/> accessed 1 April 2015.
460 See for example: 'Biopunk.org' (*Biopunk.org*) <http://www.biopunk.org/> accessed 31 March 2015; 'The Open Biohacking Project/Kit' (*Biohack*) <http://biohack.sourceforge.net/> accessed 31 March 2015; 'Welcome to Genspace' (*Genspace*) <http://genspace.org/> accessed 31 March 2015; 'An Institution for the Do-It-Yourself Biologist' (*DIYbio*) <http://diybio.org/> accessed 31 March 2015.
461 Ariana Eunjung Cha, 'Glowing Plant Project on Kickstarter Sparks Debate about Regulation of DNA Modification' *The Washington Post* (4 October 2013) <http://www.washingtonpost.com/national/health-science/glowing-plant-project-on-kickstarter-sparks-debate-about-regulation-of-dna-modification/2013/10/03/e01db276-1c78-11e3-82ef-a059e54c49d0_story.html> accessed 1 April 2015.
462 Catherine Rhodes, *International Governance of Biotechnology: Needs, Problems and Potential* (A&C Black 2010) 90. Further support for this position can be found in: Meredith Wadman, 'US Drafts Guidelines to Screen Genes' [2009] Nature News <http://www.nature.com/news/2009/091204/full/news.2009.1117.html> accessed 1 April 2015; 'Wilson Center Participating in UK Synthetic Biology Initiative' (*Synthetic Biology Project*, 3 February 2014) <http://www.synbioproject.org/news/project/6677/> accessed 1 April 2015; Peter Aldhous, 'The Bioweapon Is in the Post' [2005] *New Scientist* <http://www.newscientist.com/article/mg18825252.900-the-bioweapon-is-in-the-post.html> accessed 1 April 2015.
463 European Group on Ethics in Science and New Technologies, 'Ethics of Synthetic Biology' (2009) Opinion No 25 48–54 <https://www.erasynbio.eu/lw_resource/datapool/_items/item_15/ege__opinion25_en.pdf> accessed 31 March 2015. See, for example, recommendations 2, 5, 14, 15, 18, 20
464 Presidential Commission for the Study of Bioethical Issues, 'New Directions: The Ethics of Synthetic Biology and Emerging Technologies' (2010) 132 <http://bioethics.gov/sites/default/files/PCSBI-Synthetic-Biology-Report-12.16.10_0.pdf> accessed 31 March 2015. See recommendation 8.
465 See 5.3.5

understanding of the potential applications and the associated risks and benefits of synthetic biology, which is overviewed in the remainder of this section. In section 4.2 I briefly detail DNA design work, the populations partaking in this activity, and the challenges to regulation posed therein. In section 4.3 I outline the current regulations relevant to synthetic biology, examining their impact on DNA design research and products by drawing on the story of the 'Glowing Plants Project' as a mini case study. Section 4.4 examines and compares the two industry-led regulatory initiatives that I suggest should form a central part of gene synthesis regulation: the International Association Synthetic Biology (IASB) Code of Conduct[466] and the International Gene Synthesis Consortium (IGSC) Harmonized Screening Protocols.[467] In section 4.5 I explain 'risk-based regulation', and consider the regulatory 'fit' between this approach and the two regulatory initiatives developed by the industry. Finally, section 4.6 comprises my concluding thoughts.

4.1.1 Synthetic biology: benefits, risks & applications

It is anticipated that the creation of new biological entities will find practical applications in fields as diverse as medicine, energy, and agriculture. In the field of medicine advances in synthetic biology can benefit the entire 'therapeutic spectrum':[468] from identifying and understanding pathologies and pathological behaviours using synthetic frameworks, to developing and delivering effective, targeted therapies (e.g. equipping therapeutic drugs to combat antibiotic resistance, and designing cancer therapies that accurately detect and attack cancer cells).[469] Perhaps the greatest success story of synthetic biology to date is the development and production of semi-synthetic *Artemisia annua*, a rare plant extract that is an essential ingredient in the anti-malarial drug, Artemisinin.[470]

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466 IASB (n 451).
467 IGSC (n 451).
468 Ahmad S Khalil and James J Collins, 'Synthetic Biology: Applications Come of Age' (*Nature Reviews: Genetics*, July 2011) <http://www.nature.com/nrg/posters/synbioapps/synbioapps.pdf> accessed 1 April 2015.
469 Ibid; Ahmad S Khalil and James J Collins, 'Synthetic Biology: Applications Come of Age' (2010) 11 Nature Reviews Genetics 367.
For an account of synthetic biology advances in the field of (bio)medicine also see: Wilfried Weber and Martin Fussenegger, 'Emerging Biomedical Applications of Synthetic Biology' (2012) 13 Nature Reviews Genetics 21.
470 Chris J Paddon and Jay D Keasling, 'Semi-Synthetic Artemisinin: A Model for the Use of Synthetic Biology in Pharmaceutical Development' (2014) 12 Nature Reviews Microbiology 355. See also: Vincent JJ Martin and others, 'Engineering a Mevalonate Pathway in Escherichia Coli for Production of Terpenoids' (2003) 21 Nature Biotechnology 796; Dae-Kyun Ro and others, 'Production of the Antimalarial Drug Precursor Artemisinic Acid in Engineered Yeast' (2006) 440 Nature 940; CJ Paddon

In the field of energy and resources, synthetic biology has the potential to produce greener, cleaner, cheaper, biofuels.[471] In the United States in particular, there has been a significant investment in the development of carbon-neutral energy from both the public and private sector; for example, the production of ethanol from cellulose.[472] Synthetic biology can also be used to develop biosensors that can detect contaminants such as arsenic and mercury,[473] or to develop bioremediation systems that degrade toxic/unwanted material from the natural environment (e.g. cleaning up oil-spills).[474] More recently, synthetic biology techniques have been used to demonstrate the production of isobutanol,[475] fatty acid-based biodiesels[476] and gasoline,[477] bringing us closer to the synthetic production of energy.[478] In fact, synthetic biology offers the potential to produce, in a cost-effective way, any natural resource, no matter how rare or complex, from fuels to food – or indeed, to concoct entirely novel resources and materials.[479]

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and others, 'High-Level Semi-Synthetic Production of the Potent Antimalarial Artemisinin' (2013) 496 Nature 528.

471 United States Department of Energy, Biological and Environmental Research Advisory Committee, 'Synthetic Genomes: Technologies and Impact' (2004) <http://science.energy.gov/~/media/ber/berac/pdf/Syn_bio.pdf> accessed 31 March 2015. See also: Kelly Drinkwater and others, 'Creating a Research Agenda for the Ecological Implications of Synthethic Biology' (Wilson Center; Synthetic Biology Project; MIT Program on Emerging Technologies 2014) SYNBIO 7 <http://www.wilsoncenter.org/sites/default/files/SYNBIO_res_agenda.pdf> accessed 1 April 2015.

472 Lee R Lynd and others, 'Consolidated Bioprocessing of Cellulosic Biomass: An Update' (2005) 16 Current opinion in biotechnology 577; US Department of Energy, 'Breaking the Biological Barriers to Cellulosic Ethanol: A Joint Research Agenda' (2006) DOE/SC-0095 <http://genomicscience.energy.gov/biofuels/2005workshop/b2blowres63006.pdf> accessed 31 March 2015; DOE Office of Biological & Environmental Research, 'Biofuels Strategic Plan' (2009) <http://science.energy.gov/~/media/ber/pdf/Biofuels_strategic_plan.pdf> accessed 31 March 2015. For an overview of private investors see: ETC Group (n 447) 27.

473 Christopher E French and others, 'Synthetic Biology and the Art of Biosensor Design', *Institute of Medicine (US) Forum on Microbial Threats* (National Academies Press US 2011) <http://www.ncbi.nlm.nih.gov/books/NBK84465/> accessed 1 April 2015.

474 Charles W Schmidt, 'Synthetic Biology: Environmental Health Implications of a New Field' (2010) 118 Environmental Health Perspectives A118; Víctor de Lorenzo, 'Systems Biology Approaches to Bioremediation' (2008) 19 Current Opinion in Biotechnology 579.

475 Shota Atsumi, Taizo Hanai and James C Liao, 'Non-Fermentative Pathways for Synthesis of Branched-Chain Higher Alcohols as Biofuels' (2008) 451 Nature 86; Yi-Xin Huo and others, 'Conversion of Proteins into Biofuels by Engineering Nitrogen Flux' (2011) 29 Nature Biotechnology 346.

476 Eric J Steen and others, 'Microbial Production of Fatty-Acid-Derived Fuels and Chemicals from Plant Biomass' (2010) 463 Nature 559.

477 Yong Jun Choi and Sang Yup Lee, 'Microbial Production of Short-Chain Alkanes' (2013) 502 Nature 571.

478 D Ewen Cameron, Caleb J Bashor and James J Collins, 'A Brief History of Synthetic Biology' (2014) 12 Nature Reviews Microbiology 381.

479 Parliamentary Office of Science and Technology, 'Synthetic Biology' (2008) POST note 298 <http://www.parliament.uk/documents/post/postpn298.pdf> accessed 31 March 2015.

Synthetic biology is still working towards practical applications; most synthetic biology stories that have hit the headlines focus on progress made in the laboratory.[480] At the level of fundamental science, research in synthetic biology, such as the examples cited above, is contributing to a better understanding of biological systems.[481] A recent history of the field observed:

> 'In many aspects, the trajectory of the field during its first decade of existence has been non-linear, with periods of meaningful progress matched by episodes of inertia as design efforts have been forced to re-orient when confronted with the complexity and unpredictability of engineering inside living cells.'[482]

However, for all the potential benefits of synthetic biology, in terms of knowledge and (future) applications, there are, of course, potential risks and harms. For, synthetic biology presents the classic dual-use dilemma – 'a technology with broad and varied beneficial applications, but one that could also be turned to nefarious, destructive use'.[483] The quote continues:

> 'Such technologies have been around ever since the first humans picked up rocks or sharpened sticks. But biology brings some unique dimensions: given the self-propagating nature of biological organisms and the relative accessibility of powerful biotechnologies, the means to produce a 'worst case' are more readily attainable than for other technologies.'[484]

The risks and potentials harms associated with synthetic biology may be divided into two categories: ethical/non-physical[485] and physical. The latter is the focus of this

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480 Most notably: 'Press Release - First Self-Replicating, Synthetic Bacterial Cell Constructed by J. Craig Venter Institute Researchers' (*J Craig Venter Institute*, 20 May 2010) <http://www.jcvi.org/cms/press/press-releases/full-text/article/first-self-replicating-synthetic-bacterial-cell-constructed-by-j-craig-venter-institute-researcher/home/> accessed 31 March 2015; Annaluru and others (n 456); Denis A Malyshev and others, 'A Semi-Synthetic Organism with an Expanded Genetic Alphabet' (2014) 509 Nature 385.

481 The famous 'last words' of Richard Feynman, found scrawled across his blackboard at Caltech at the time of his death read - 'what I cannot create, I do not understand'. (Richard Feynman, '1.10-29.jpg (JPEG Image, 463 × 326 Pixels)' (*Caltech Archives*, 1988) <http://archives.caltech.edu/pictures/1.10-29.jpg> accessed 1 April 2015.) These words were watermarked into the first self-replicating, synthetic bacterial cell created by J Craig Venter and his team, ('Press Release - First Self-Replicating, Synthetic Bacterial Cell Constructed by J. Craig Venter Institute Researchers' (n 480).) indeed the sentiment captured in Feynman's words resonates throughout the synthetic biology community.

482 Cameron, Bashor and Collins (n 478).

483 Michele S Garfinkel and others, 'Synthetic Genomics: Options for Governance' (2007) 3 Industrial Biotechnology 333, 1.

484 Ibid; Caitríona McLeish and Paul Nightingale, 'Biosecurity, Bioterrorism and the Governance of Science: The Increasing Convergence of Science and Security Policy' (2007) 36 Research Policy 1635.

485 Erik Parens, Josephine Johnston and Jacob Moses, 'Ethical Issues in Synthetic Biology' (The Hastings Centre 2009) Synbio 3 <http://www.synbioproject.org/process/assets/files/6334/synbio3.pdf> accessed 31 March 2015.

chapter – the protocols are designed to prevent physical harms from manifesting. However, as ethics are an important consideration throughout the regulatory cycle,[486] in the interests of thoroughness it is important to acknowledge both sets of risk/harm.

Considering the ethical dimension first, on one hand are arguments outlining the moral obligation to pursue this biotechnology: progress in this field could lead to significant therapeutic benefits for humanity and the environment (as enumerated above) and even accelerate human enhancement and evolution.[487] On the other hand are the moral objections: (i) concerns over the hubris of mankind attempting to 'play God' and/or) interfering with Nature and the evolutionary process,[488] (ii) eroding the distinction between living organisms and machines, thus raising questions over the moral status of synthetic or semi-synthetic organisms (versus natural organisms) [489] and (iii) the dangers of disseminating knowledge that might be misused.[490]

The second category of risks/detriments associated with synthetic biology is the potential physical risk posed to human and animal health/well-being and the environment by the introduction of novel organisms (by accident or design) into our natural systems/environment – an argument that inherits much from the on-going GM debate.[491] Specific to synthetic biology are the risks posed by the potential this technology offers to build a new generation of bioweapons, the danger of bioterrorism,

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[486] See chapter II

[487] John Harris, *Enhancing Evolution: The Ethical Case for Making Better People* (Princeton University Press 2010).

[488] CAJ Coady, 'Playing God' in Julian Savulescu and Nick Bostrom (eds), *Human Enhancement* (Oxford University Press 2009); Peter Dabrock, 'Playing God? Synthetic Biology as a Theological and Ethical Challenge' (2009) 3 Systems and synthetic biology 47.

[489] Anna Deplazes and Markus Huppenbauer, 'Synthetic Organisms and Living Machines' (2009) 3 Systems and synthetic biology 55; Anna Deplazes-Zemp, 'The Moral Impact of Synthesising Living Organisms: Biocentric Views on Synthetic Biology' (2012) 21 Environmental Values 63; Mildred K Cho and others, 'Ethical Considerations in Synthesizing a Minimal Genome' (1999) 286 Science 2087.

[490] Thomas Douglas and Julian Savulescu, 'Synthetic Biology and the Ethics of Knowledge' (2010) 36 Journal of medical ethics 687; Robin L Pierce, 'Whose Ethics of Knowledge? Taking the next Step in Evaluating Knowledge in Synthetic Biology: A Response to Douglas and Savulescu' (2012) 38 Journal of Medical Ethics 636. For a response to the 'ethics of knowledge' argument see: Iain Brassington, 'Synthetic Biology and Public Health' (2011) 1 Theoretical & Applied Ethics.

[491] Joyce Tait, 'Upstream Engagement and the Governance of Science' (2009) 10 EMBO reports S18; Joyce Tait, 'Adaptive Governance of Synthetic Biology' (2012) 13 EMBO Reports 579; Joyce Tait, 'Governing Synthetic Biology: Processes and Outcomes' in Markus Schmidt and others (eds), *Synthetic Biology: the technoscience and its societal consequences* (Springer Netherlands 2010); David Shukman, 'Will Synthetic Biology Become a GM-Style Battleground?' (*BBC News - Science & Environment*, 12 July 2013) <http://www.bbc.co.uk/news/science-environment-23274175> accessed 1 April 2015.
See also: chapter II

and threat to biosecurity.[492] Synthetic biology renders the revival or creation of hostile organisms easier than ever before. These hostile organisms could take the form of lethal or crippling viruses or bacteria that devastate and destroy the natural environment. They may be designed to attack indiscriminately or only within targeted populations, and may be as communicable as the common cold/flu virus, as speedy as a tsunami or earthquake. Moreover, synthetic biology combined with the resources accessible online, enables the development of cheap, easy-to-assemble, DIY bioweapons.[493] For some, synthetic biology is indeed the face of modern warfare and terrorism. And then there is the unknown – consequences that we cannot yet see or fathom. These scenarios outline the 'worst-case possible' and it is important to bear in mind that these worst-case scenarios are possibilities, not certainties.

4.1.2 Why regulate synthetic biology?

Yet, if we are to pursue research in synthetic biology – and we in fact *are already doing so* – the question we return to is how to mitigate and manage these risks, for they cannot reasonably be ignored or left to chance. Here, regulation can help.[494] This chapter proceeds from the premise that current research in synthetic biology will continue to take place in the foreseeable future for several reasons: Firstly, given how widespread research in synthetic biology is, a ban on activity in this field would be difficult, if not impossible, to implement and enforce. Secondly, the potential benefits of synthetic biology research are compelling – enough to secure significant investment in this industry, in time, money and hope, from both the public and private sector. Thirdly, given that the proverbial cat is already out of the bag, the best response or remedy to an adverse event or attack caused by synthetic biology would likely rely on understanding and manipulating the technology itself. In light of the risks and complexities that pervade the field of synthetic biology I suggest regulation is necessary (or at the very least, should be explored as an option) for this technology to fulfil its potential, whilst simultaneously managing, minimizing and containing the physical risks and harms posed by on-going work in the field.[495]

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[492] ETC Group (n 447) 23; Filippa Lentzos, 'Synthetic Biology, Security and Governance' (2012) 7 BioSocieties 339.

[493] Jeffrey Marlow, 'The Next Bioweapon May Be a Text File' (*WIRED*, 1 November 2013) <http://www.wired.com/2013/11/the-next-bioweapon-may-be-a-text-file/> accessed 31 March 2015; Aldhous (n 462).

[494] See 1.3

[495] A view recently shared and published in a statement by the Inter-Academy Panel of the Global Network of Science Academies. (IAP, 'IAP Statement on Realising Global Potential in Synthetic Biology:

4.2 DNA Design: people, practices and regulatory challenges

Activity that constitutes 'synthetic biology' is as varied as it is widespread. Heavey categorizes the myriad research areas that fall under the umbrella of synthetic biology into seven primary areas; here we are concerned with only two: DNA design and DIY biology/garage biohacking (used interchangeably henceforth).[496] This section overviews the science of DNA synthesis, the research populations, and the challenges that this area of synthetic biology presents for regulation.

4.2.1 DNA design

Researchers in this field aim to create novel genomes. Whereas conventional genetic engineering/modification enables us to read and manipulate existing genetic codes, DNA design will hopefully allow us to write altogether novel DNA. Gene or DNA synthesis companies play a key role in this area, offering a speedy service that synthesizes and delivers DNA as instructed. This field has received significant media attention, perhaps because it so easily captures the imagination, but also due to the progress that has been made by researchers in this area in recent years. Firstly, there is Craig Venter's success in creating *M. mycoides,* the world's first artificial bacterium.[497] Although an artificial bacterium is not as exciting as, say, a hippogriff, the underlying principles and process are the same: Venter and his team decoded the genome of the *Mycoplasma mycoides* bacterium, created a synthetic copy of the DNA sequence and inserted it into the *Mycoplasma capricolum* bacterium cell. The cell self-replicated expressing the synthetic DNA[498] providing a ground-breaking proof-of-concept that could one day be used to create more complex living organisms, such as the hippogriff.

Scientific Opportunities and Good Governance' (2014) <http://www.interacademies.net/File.aspx?id=23974> accessed 31 March 2015.) In a parallel commentary co-chair Volker ter Meulen called for the urgent development of 'policies on synthetic biology [that] set out sensible practices to mitigate the risk that is inherent in any major advance, yet are flexible enough to encourage research and innovation.' (Volker ter Meulen, 'Time to Settle the Synthetic Controversy' (2014) 509 Nature 135.) I submit that new governance can help achieve precisely that – see 1.2.1, 1.4, 5.2, 5.3

[496] Heavey (n 449) 18–36. The areas are: DNA design, minimal microbe genome, enhancing the genetic code, building artificial cells, metabolic/pathway engineering, living machines, and DIY biology/garage biohacking.

[497] 'Press Release - First Self-Replicating, Synthetic Bacterial Cell Constructed by J. Craig Venter Institute Researchers' (n 480); Daniel G Gibson and others, 'Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome' (2010) 329 science 52.

[498] Gibson and others (n 497).

Secondly, four years on Professor Jef Boeke (Director of New York University Langone Medical Center Institute for Systems Genetics) and his team hit the international news headlines with their announcement of the creation of a functioning synthetic yeast chromosome.[499] Boeke and his team first downloaded the DNA sequence of the yeast species *Saccharomyces cerevisiae* (commonly known as bakers or brewers yeast). Work then began on the smallest of the 16 chromosomes (chromosome lll) – removing 'junk' DNA and reorganizing the sequence. The 'edited' sequence, named *synlll*, was then divided into sections that were chemically synthesized and finally assembled by 60 undergraduate students at Johns Hopkins University. The original chromosome was then replaced with *synlll* in the yeast cell; happily, the cell functioned as normal.[500] This is one step in the grander project of synthesizing the entire *Saccharomyces cerevisiae* genome. The achievement moves the field forward by demonstrating success in working with a more complex eukaryotic organism (containing a nucleus), and has been applauded by scientists, including Venter.[501] In addition to the deeper understanding of DNA design and manipulation that is to be gained, this advance brings the field closer to developing applications such as synthetic vaccines and biofuels.[502]

Thirdly, work carried out and supported by the BioBricks Foundation, founded by Drew Endy and colleagues, has drawn significant attention. The concept of BioBricks is to 'design DNA parts that perform specific functions [which] can be combined with other parts to perform composite functions…[and] then be added to a bacterium to change its function'.[503] Thus, as Drew Endy explains, hopefully one day we will be able to grow houses from trees.[504] The philosophy behind the BioBricks Foundation is to maintain an open source, non-commercial, free library of standardized biological parts, i.e. the 'BioBricks'[505] to encourage the development of practical applications through synthetic biology:

> 'Our mission is to ensure that the engineering of biology is conducted in an open and ethical manner to benefit all people and the planet.

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499 Annaluru and others (n 456).
500 Daniel G Gibson and J Craig Venter, 'Synthetic Biology: Construction of a Yeast Chromosome' (2014) 509 Nature 168; Baker (n 456).
501 Gibson and Venter (n 500).
502 Ibid; Baker (n 456).
503 Heavey (n 449) 19.
504 ETC Group (n 447) 16.
505 'The BioBrick™ Public Agreement' (*BioBricks Foundation*) <https://biobricks.org/bpa/> accessed 31 March 2015; 'Registry of Standard Biological Parts' (*iGEM*) <http://parts.igem.org/Main_Page> accessed 31 March 2015.

> We envision a world in which scientists and engineers work together using freely available standardized biological parts that are safe, ethical, cost effective and publicly accessible to create solutions to the problems facing humanity.'[506]

The BioBricks Foundation runs an annual competition, iGEM (International Genetically Engineered Machine Competition) for science students (high school and undergraduate).[507]

4.2.2 DIY biology

Arguably the most fascinating and intriguing research in synthetic biology is not work that is undertaken at major research institutions and published in international, peer reviewed journals, but the research undertaken outside the 'mainstream' research community in the underground world of DIY biology.

Reminiscent of the early years in Silicon Valley when a lot of innovation came from the garages and bedrooms of teenage hackers,[508] garage biohacking is growing global movement. DIY synthetic biologists set up laboratories at home, use a hackerspace,[509] community lab, or even a corporate, government or academic lab.[510] They also take advantage of the opportunities and mobility offered via the internet. This trend has a definite, vibrant presence online,[511] with biohackers sharing and discussing methods, tools, stratagems, and results for both the novice and experienced enthusiast. There are even courses in biohacking.[512] This is not a discrete technical area of research; work undertaken by garage scientists can fall under any area of synthetic biology including DNA design. However, it's accessibility renders DNA design the technology of choice

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506 'About - BioBricks Foundation' (*BioBricks Foundation*) <http://biobricks.org/about-foundation/> accessed 31 March 2015.

507 'Main Page - 2014.igem.org' (*iGEM 2014*) <http://2014.igem.org/Main_Page> accessed 31 March 2015; 'Main Page - 2015.igem.org' (*iGEM 2015*) <http://2015.igem.org/Main_Page> accessed 31 March 2015.

508 Robert X Cringely, *Accidental Empires: How the Boys of Silicon Valley Make Their Millions, Battle Foreign Competition, and Still Can't Get a Date* (HarperBusiness 1996); Steven Levy, 'Geek Power: Steven Levy Revisits Tech Titans, Hackers, Idealists' (*WIRED*, 19 April 2010) <http://www.wired.com/2010/04/ff_hackers/> accessed 31 March 2015.

509 'A hackerspace (also called a makerspace) is a community workspace where people gather, socialize, and collaborate on computers, technology, and science projects' - Daniel Grushkin, Todd Kuiken and Piers Millet, 'Seven Myths and Realities of Do-It-Yourself Biology' (Wilson Center; Synthetic Biology Project 2013) Synbio 5 5 <http://www.synbioproject.org/process/assets/files/6676/7_myths_final.pdf> accessed 31 March 2015.

510 Grushkin, Kuiken and Millet (n 509); Günter Seyfried, Lei Pei and Markus Schmidt, 'European Do-It-Yourself (DIY) Biology: Beyond the Hope, Hype and Horror' (2014) 36 Bioessays 548.

511 'Biopunk.org' (n 460); 'The Open Biohacking Project/Kit' (n 460); 'An Institution for the Do-It-Yourself Biologist' (n 460); 'Welcome to Genspace' (n 460). In addition to formally dedicated spaces such as these, personal social media forums provide a space for DIY biologists to work and socialize.

512 'Welcome to Genspace' (n 460).

for biohackers[513] – between open source projects such as BioBricks, and the plethora of gene synthesis companies that have emerged, the decreasing costs of reading and writing DNA and investing in equipment (for example, purchasing from Ebay),[514] bio-building is a remarkably accessible hobby, or even full/part-time profession.

The Glowing Plant Project[515] (see further 4.3.2) is an example of what can be achieved through DIY DNA design. This project, to develop seeds that produce glow-in-the-dark plants, was conducted by independent scientists/entrepreneurs working out of converted shipping container,[516] financed through online crowd-funding,[517] and engaged the services of a private gene synthesis company.[518] DIY synthetic biology, as exemplified by the Glowing Plant Project can be a highly sophisticated, wide-reaching, and powerful enterprise. In designing regulatory systems, this population must be carefully considered as they operate outside mainstream channels of funding, laboratory operations, and peer-review that offer some form of oversight.[519] This community is beginning to appear on regulators' radars, prompted by projects such as the GPP.[520]

Finally, activity in synthetic biology is only part of biohacking community and culture, but it is anticipated that as the field develops so too will its popularity and import throughout the biohacking community.[521]

4.2.3 Challenges for regulation

Synthetic biology is a rapidly expanding field; a worldwide analysis by the Synthetic Biology Project demonstrates significant growth in the field, within both the private and public sector.[522] It is predicted that the global market value for synthetic biology will

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513 Ben Beaumont-Thomas, 'How to Make a Biohack Lab' (*WIRED.CO.UK*, 21 February 2012) <http://www.wired.co.uk/magazine/archive/2012/03/how-to/make-a-biohack-lab> accessed 31 March 2015.
514 Grushkin, Kuiken and Millet (n 509).
515 'Glowing Plant: Natural Lighting without Electricity' (n 443).
516 Cha (n 461).
517 'Glowing Plants: Natural Lighting with No Electricity' (*Kickstarter*) <https://www.kickstarter.com/projects/antonyevans/glowing-plants-natural-lighting-with-no-electricit> accessed 31 March 2015.
518 Cha (n 461).
519 Todd Kuiken, 'Beyond the Lab and Far Away: A View from Washington' [2014] BioCoder <http://www.oreilly.com/biocoder/> accessed 1 April 2015. (Paid download)
520 Ibid; Grushkin, Kuiken and Millet (n 509).
521 Heavey (n 449) 28.
522 The Wilson Center, 'Tracking the Growth of Synthetic Biology: Findings for 2013' (2013) <https://www.cbd.int/doc/emerging-issues/emergingissues-2013-07-WilsonCenter-Synbio_Maps_Findings-en.pdf> accessed 31 March 2015.

grow from $1.6bn in 2011 to $10.8bn by 2016.[523] Investment in the field – financial and political – represents the hope and opportunity that synthetic biology provides to solve many of the world's problems and enhance our experience on Earth. However, as we have seen, alongside its potential benefits are potential risks (e.g. bio-error, bioterror) that are cause for legitimate concern.

Managing these risks would be prudent, but directly regulating *every single* synthetic biologist and *every single* instance of synthetic biology work is an unrealistic if not impossible task. Choices then must be made as to what to regulate, who to regulate and *how* to regulate. DNA design is one of the more accessible fields within synthetic biology due to the key role that commercial gene synthesis companies play – synthesized DNA is available to anyone, anywhere in the world, willing to pay. DNA design, as well as being a relatively advanced study within synthetic biology, is also popular amongst a variety of actors, from academicians to hobbyists - it is not limited by the need for expensive laboratory equipment or space. These factors together raise the risk profile of DNA design. Even so, regulating every single DNA design researcher and every single instance of DNA design work is still an unrealistic, if not impossible, task.

Regulatory efforts can be focussed: targeting commercial gene sequencing limits dangerous DNA design projects through monitoring the type of gene sequences generated and sold, and the type of end user to whom they are sold. Here, the *highest* risks are pursued, rather than every potential risk. This approach – RBR – offers a pragmatic solution to the task of regulating a wide-reaching and diverse field. This framework will be explored further in sections 4.4 and 4.5. For now, it is necessary to consider the scope of regulations that currently govern synthetic biology, and particularly DNA synthesis.

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[523] UK Synthetic Biology Roadmap Coordination Group, 'A Synthetic Biology Roadmap for the UK' (2012) 4 <http://www.rcuk.ac.uk/RCUK-prod/assets/documents/publications/SyntheticBiologyRoadmap.pdf> accessed 31 March 2014.
See also the following maps that track synthetic biology activity around the world: 'Synthetic Biology Map' (*Synthetic Biology Project*) <http://www.synbioproject.org/sbmap/> accessed 31 March 2015; 'Global Map of Synthetic Biology' (*IASB*) <http://www.ia-sb.eu/go/synthetic-biology/activities/press-area/press-information/global-map-of-synthetic-biology/> accessed 31 March 2015.

4.3 The international network of regulations covering synthetic biology

4.3.1 Current regulations

To date, there are no specific, hard laws governing synthetic biology. Following JCVI's announcement in May 2010, President Obama's Commission for the Study of Bioethical Issues published a report in December 2010, *New Directions: The Ethics of Synthetic Biology and Emerging Technologies*.[524] The report outlined eighteen specific recommendations that fall into the categories of risk assessment, oversight, coordination, research, education and ethics to have been completed by June 2012. The Woodrow Wilson Centre has kept a 'score card' of progress;[525] to date not a single recommendation has been completely fulfilled, and on four of the eighteen recommendations government has taken no action at all.[526] In fact, the report stated that:

> 'The Commission sees no need at this time to create additional agencies or oversight bodies focused specifically on synthetic biology. Rather, the Commission urges the Executive Office of the President, in consultation with relevant federal agencies, to develop a clear, defined, and coordinated approach to synthetic biology research and development across the government.'[527]

A similar sentiment can be found in Europe. The European Group on Ethics urged the European Commission as early as 2009 to consider the need for specific regulations, and expand current regulation, to cover the spectrum of synthetic biology work.[528] No specific regulations have emerged. The EC are currently consulting on the issue of synthetic biology in a series of three opinions.[529]

Yet, to say that 'the 'artificial life industry' is growing up in a 'Wild West' free-for-all environment with virtually no regulatory oversight' [530] is misleading. Synthetic biology

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[524] Presidential Commission for the Study of Bioethical Issues (n 464).
[525] 'Synthetic Biology Scorecard: Introduction to the Project' (*Synthetic Biology Project*) <http://www.synbioproject.org/scorecard/> accessed 31 March 2015. (Recommendation 8)
[526] 'Overview of Recommendations' (*Synthetic Biology Project*) <http://www.synbioproject.org/scorecard/recommendations/> accessed 31 March 2015.
[527] Presidential Commission for the Study of Bioethical Issues (n 464) 8.
[528] European Group on Ethics in Science and New Technologies (n 463) 48–54. See, for example, recommendations 1, 3, 9, 10, 11, 13, 19
[529] Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks and Scientific Committee on Consumer Safety, 'Opinion on Synthetic Biology I: Definition' (n 445); Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks and Scientific Committee on Consumer Safety, 'Preliminary Opinion on Synthetic Biology II: Risk Assessment Methodologies and Safety Aspects' (2014) <http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_048.pdf> accessed 31 March 2015.
[530] ETC Group (n 447) 4.

activity is caught in by web of regulations at different levels.[531] National and regional regulations that govern the production and distribution of genetically modified organisms also apply to synthetic biology. Applications developed using synthetic biology would be governed by regulations relevant to product produced, for example, medicines and pharmaceuticals, dangerous chemicals, nuclear technologies, atomic technologies, cloning and research on animals to name a few areas. This chapter focuses on the international dimension of governance (see 5.3.5) and at this level too, there are number of relevant legal international regulations. The following table (Table E) sets out these regulations and summarises the scope of applicability to synthetic biology.

[531] This was recently reiterated by ter Meulen: 'The recognition that key methods are already controlled is crucial, because it should defuse some of the public controversy about risk. Also important is striking the right balance between statutory regulation and self-governance by scientists and scientific bodies. (The IAP and others have published recommendations on how to develop individual and institutional codes of conduct.).' (ter Meulen (n 495). Choosing the appropriate regulatory approaches/tools and balance between regulatory approaches/tools is a key theme within this thesis; see further: chapter III (viz. international stem cell research), 1.4, 4.5, 5.3

TABLE E: Legally binding regulations

Regulation	Applicability
Geneva Protocol[532]	Prohibits the use of chemical and biological weapons in warfare
Biological Weapons Convention[533]	Prohibits the development, production, stockpiling, acquisition, retention or transfer of biological weapons
Chemical Weapons Convention[534]	Prohibits the production, stockpiling, and use of chemical weapons and precursors.
UN Security Council Resolution 1540[535]	Requires all states to take measures against the proliferation and delivery of weapons of mass destruction, including biological weapons.
Cartagena Protocol[536] (Discussions are currently underway exploring the implications synthetic biology has on the Convention[537])	Regulates the transfer, handling and use of living modified organisms through the operation of a precautionary principle based approach
Nagoya Protocol[538]	Provides a legal framework for the 'fair and equitable sharing of benefits arising out of the utilization of genetic resources', and thereby fulfilling the capacity building objective of the CBD
Nagoya-Kuala Lumpur Supplementary Protocol[539]	Addresses matters of liability and redress due to damage caused by the transboundary movement of living modified organisms

[532] Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare (signed on 17 June 1925, entered into force on 8 February 1928) Geneva, Switzerland

[533] Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (adopted 3 September 1992, opened for signature 10 April 1972, entered into force 26 March 1975) London, Moscow, Washington D.C.

[534] Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on Their Destruction (opened for signature in Paris on 13 January 1993 and entered into force on 29 April 1997) Paris, New York

[535] UNSC Res 1540 (28 April 2004) UN Doc S/RES/1540

[536] Secretariat of the Convention on Biological Diversity (2002), Cartagena Protocol on Biosafety to the Convention on Biological Diversity: text and annexes (adopted 29 January 2000, entered into force 11 September 2003) Montreal, Canada

[537] 'New & Emerging Issues' (*Convention on Biological Diversity*) <https://www.cbd.int/emerging/> accessed 31 March 2015.

[538]Secretariat of the Convention on Biological Diversity, Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (adopted on 29 October 2010, entered into force on 12 October 2014) Nagoya, Japan

[539] Secretariat of the Convention on Biological Diversity, Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety (signed 15 October 2010, not yet entered into force) Nagoya, Japan

There are also a number documents, developed by various organisations and non-binding in nature, that offer guidance for those in the synthetic biology field:

TABLE F: Non-legally binding regulations and guidance

Organisation	Regulation	Applicability
Australia Group	Guidelines for Transfers of Sensitive Chemical or Biological Items (June 2012)	Seeks to control the export of material and technology that may contribute to the development of biological or chemical weapons
World Health Organisation (WHO)	Biosafety Manual, 3rd Edition (2004)	Provides guidance on biosafety in the laboratory, including conducting risk assessments
WHO	Laboratory Biosecurity Guidance (September 2006)	Provides guidance on managing biorisks; including detailed guidance on matters of biosecurity
IASB	Code of Conduct for Best Practices in Gene Synthesis (November 2009)	Provides gene synthesis companies a framework for screening gene sequence orders
IGSC	Harmonized Screening Protocol (November 2009)	Provides gene synthesis companies a framework for screening gene sequence orders
International Risk Governance Council (IRGC)	Risk governance of synthetic biology – concept note (2009)	Sets out background and agenda for developing a risk governance framework
IRGC	Guidelines for the Appropriate Risk Governance of Synthetic Biology – policy brief (2010)	Develops the concept of appropriate risk governance and provides guidance on balancing competing interests of enabling innovation, and minimizing risks to people and the environment
Synbio 2.0	Community Declaration (2006)	Failed: no result
J. Craig Venter Institute; Center for Strategic & International Studies; Massachusetts Institute of Technology	Synthetic Genomics: Options for Governance (October 2007)	Explores governance options to ensure biosecurity, laboratory safety, and protect the communities and environment outside of laboratories; aimed at commercial DNA suppliers, oversight of DNA synthesis, and end users.

In 4.4 I return to look at the IASB and IGSC documents in detail, examining their potential as a basis for formal risk-based regulation. These documents are focussed on as they provide specific practical guidance and are in operation. For now, I consider the impact of the current state of regulation on gene synthesis activity. A good demonstration of this can be found in the story of the Glowing Plant Project (GPP) that attracted considerable worldwide media attention in 2013.

4.3.2 The impact of regulation & the Glowing Plant Project

The GPP brought to light the fact that a product of synthetic biology engineering could be released, unchecked, yet legally, into the environment, prompting questions over the suitability of current regulations to cope with synthetic biology.

Shortly after GPP launched on Kickstarter, the environmental activist organization, ETC Group, launched a counter-campaign - 'Kickstopper'.[540] Their goal was to '…stop US biohackers and private biotech firm, Genome Compiler Corporation, from carrying out the first ever, intentional release of organisms created through synthetic biology.'[541] They cite, as reasons for their opposition to synthetic biology, and the GPP in particular, the potential ecological risks, biosafety concerns, the young and experimental nature of synthetic biology, and the absence of governmental oversight for development, field release and commercial use of synthetic biology products. Here, I focus on the regulatory issues, arguing that regulation can be used to manage the risks pointed out by the ETC, and encourage responsible science rather than stifling innovation in the field.

Urging extreme caution, the ETC lobbied Kickstarter to withdraw approval of the GPP, and government (namely, the United States Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS)) to issue an immediate moratorium on the field release and commercial use of synthetic biology organisms, and to develop appropriate laws for risk assessment, monitoring and controls targeted at the synthetic biology industry. They were only semi-successful: Kickstarter amended its rules to include genetically modified organisms on the list of items that are prohibited as

[540] 'Kickstopper! Putting a Stop to Synthetic Biology Pollution' (*ETC Group*) <http://www.etcgroup.org/kickstopper> accessed 31 March 2015.
[541] 'Let's Stop the Glowing Plant Release Project! - Only 10 Days Left to Contribute to ETC Group's Campaign' (*ETC Group*, 10 July 2013) <http://www.etcgroup.org/content/lets-stop-glowing-plant-release-project-only-10-days-left-contribute-etc-groups-campaign> accessed 31 March 2015.

a reward for donors (although the change of rules does not affect the GPP as the amendment has no retroactive application).[542] Despite the widespread media attention that GPP received, and the ETC's extensive lobbying efforts there has been no action at the governmental level to revise the current laws, or introduce new laws specifically targeting synthetic biology.

The distribution of the bioengineered glowing plant and glowing plant seeds is, at present, legal.[543] Although a number of US governmental agencies oversee matters of genetic engineering, their jurisdiction is not comprehensive enough to include novel methods of bioengineering such as those practiced by the GPP: The USDA, which regulates plant and agriculture impact through APHIS, have established guidelines for determining the level of testing required for genetically engineered crops; however the methodology used by the GPP renders the project outside the purview of the USDA. The Environmental Protection Agency (EPA) regulates the use of pesticides, but as the glowing plant will not be engineered to resist pesticides or herbicides, the EPA rules do not apply. Likewise, the Food and Drug Administration (FDA) rules do not apply as the glowing plant is intended for ornamental purposes, and not human or animal consumption.[544] Similarly, the Department of Interior's Bureau of Land Management and Fish and Wildlife Services both consider the matter outside their jurisdiction.[545] Nor are any international laws are applicable in this instance.

Interestingly, although the gene synthesis companies used by the GPP do enact gene sequence screening,[546] this layer of oversight was not mentioned in the media coverage of the story, by the GPP team, or the ETC. The discussions and debate on matters of regulation focussed squarely on 'hard laws'.

One reason for the distinct lack of governmental interest in commencing regulatory action could be that the GPP actually presents little real risk of cross-pollination and environmental destruction. The *Arabidopsis* plant is not a native plant to the United

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[542] 'Prohibited Items' (*Kickstarter*) <https://www.kickstarter.com/rules/prohibited> accessed 31 March 2015; Duncan Geere, 'Kickstarter Bans Project Creators from Giving Away Genetically-Modified Organisms' (*The Verge*, 2 August 2013) <http://www.theverge.com/2013/8/2/4583562/kickstarter-bans-project-creators-from-giving-GMO-rewards> accessed 1 April 2015.
[543] The GPP are continuing to refine their design; a shipment date for seeds and plants to donors and buyers is yet to be announced ('Glowing Plant: Natural Lighting without Electricity' (n 443).)
[544] 'Glowing Plants: Natural Lighting with No Electricity' (n 517). (Under: *Is it legal?*)
[545] Cha (n 461).
[546] Personal email correspondence; N Hyder-Rahman & GPP; 7 August 2014.

States (where the GPP is being developed and eventually distributed) and has few native relatives – it will not be in its ideal reproducing environment. Also, *Arabidopsis* is a self-pollinating plant, as opposed to relying on wind or insects for pollination, which reduces the chances of uncontrolled reproduction. These factors together mean that there is little risk of cross-pollination.[547] Moreover, as the plant has been manipulated it is rendered weaker than native plant varieties, and weaker than other genetically engineered plants (most of which are specifically developed to be more resilient than wild plants) and therefore at a reproductive disadvantage. Finally, the GPP are investigating building certain safety mechanisms into the plant itself:

> 'We are currently looking into other built-in safety mechanisms. For example, there are vitamin deficient versions of arabidopsis [sic.] that have to have their daily vitamins in order to survive.'[548]

For now then, the risk of waking up in a world without a light-switch is minimal. In this sense, the absence of regulatory intervention is in line with the RBR model proposed here – one that is based on appropriate responses to risk. But what of future creations of DNA design that might pose some real risk? The lesson to be learned from the GPP story is, I suggest, that thoughtful regulation, rather than regulations that by luck stumble on the appropriate response, are required. By chance, the US regime for GMOs/recombinant DNA fails to capture DNA design. Within the EU, the reverse would be true: the same activity would be caught by the GMO-targeted regulation, moreover, the glowing plant seeds cannot even be shipped into the EU without going through the rigorous assessment processes.[549] In either case, falling within or outside the regulatory regime is a matter of luck, a happy or unfortunate accident, for neither jurisdiction designed their GMO laws with synthetic biology in mind.

If thoughtful regulatory action is required to hedge against risks materialising, what might it look like? As seen in Table F (above), in the absence of government oversight the synthetic biology community have explored and enacted a number of regulatory initiatives. The next section examines two of these 'soft' regulatory initiatives that are in

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[547] 'Glowing Plants: Natural Lighting with No Electricity' (n 517).
[548] Cha (n 461); 'We Are Making Glowing Plants Using Synthetic Biology and Hope to One Day Replace Streetlights with Glowing Trees. Ask Us Anything!' (*reddit*) <http://www.reddit.com/r/IAmA/related/1eed8t/we_are_making_glowing_plants_using_synthetic/> accessed 31 March 2015.
[549] See 2.3.1 on the EU regulations for GMOs

operation specifically designed to regulate DNA synthesis companies (such as the type used by the GPP) in detail and considers these measures as part of the - potentially permanent and formal - regulatory landscape.

4.4 The IASB and IGSC

4.4.1 The emergence of competing industry standards[550]

In April 2008 the newly formed International Association of Synthetic Biologists (IASB), based in Heidelberg, Germany, held a workshop to discuss steps that could be taken by the synthetic biology industry to mitigate the risks of biosecurity.[551] Present at the workshop were European and US biotech firms engaged in commercial synthetic biology (gene synthesis), researchers and experts in the field from science, law and policy. The workshop report states:

> 7. Workshop participants uniformly agreed that synthetic biology's principal risk for the immediate future was that terrorists could use artificial DNA to recreate naturally occurring pathogens like smallpox or 1918 influenza. This implies that better screening – including both extending existing methods to the handful of gene synthesis companies that do not use them and the development of more powerful, second generation technologies – are a powerful lever for managing this risk.[552]

Accordingly, one of the outcomes of the workshop was agreement from the participants to develop a set of protocols to screen customer orders (for DNA sequences) for potential biosecurity threats, and co-operate to adopt and implement these protocols. A draft Code of Conduct was written and published in late 2008.[553] However, months before the final IASB document was to be published two leading gene synthesis companies, DNA2.0 (USA) and Geneart (Germany) announced the forthcoming publication of an alternate Code of Conduct.[554] In September 2009 DNA2.0 and Geneart, together with three other leading gene synthesis companies, formed the International Gene Synthesis Consortium (IGSC).[555] In November 2009 the IASB published, as planned, the finalized Code of Conduct for Best Practices in Gene

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[550] See 3.4 for a parallel argument in the context of international stem cell research

[551] Hubert Bernauer and others, 'Technical Solutions for Biosecurity in Synthetic Biology' (2008) <http://www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_report_biosecurity_syntheticbiology.pdf> accessed 31 March 2008.

[552] Ibid 8.

[553] Markus Fischer and Stephen M Maurer, 'Harmonizing Biosecurity Oversight for Gene Synthesis' (2010) 28 Nature Biotechnology 20.

[554] Erika Check Hayden, 'Keeping Genes out of Terrorists' Hands' (2009) 461 Nature News 22.

[555] IGSC, 'IGSC Launch Announcement: World's Top Gene Synthesis Companies Establish Tough Biosecurity Screening Protocol' (19 November 2009) <http://www.genesynthesisconsortium.org/images/pdf/IGSC%20Launch%20Announcement.pdf> accessed 31 March 2015.

Synthesis ('IASB Code'),[556] and at the same time the IGSC launched their Harmonized Screening Protocol ('IGSC Protocol').[557]

So, what do these protocols say and how do they differ? Both codes screen orders and customers. Both protocols require that gene synthesis companies screen incoming orders against a 'master-list' of dangerous pathogens and risk-associated sequences that searches for sequence matches or reasonable similarities (s.6, IASB Code; s.1.3 IGSC Protocol). The two organisations compile and update the screening data base from the Australia Group's biological dual-use organisms list, the US Select Agent and Toxins list, and national/regional lists where appropriate, the IGSC cite the European Council Regulation (EC) No 428/2009,[558] for example (s.6 IASB Code; s.2.3 IGSC Protocol). This part of the process is the 'automated' step, carried out by a computer. Orders that are identified as potentially dangerous/risky are then assessed by a human; the IASB specify a 'molecular biologist' or similar subject matter expert (s.7 IASB Code) and the IGSC specify a 'human expert' (s.1.3 IGSC Protocol). Both of protocols require companies to screen all customers by requiring that potential customers provide basic identification and location details: full postal address (no PO Boxes), institution name, telephone number and email address (s.8 IASB Code; s.2.1 IGSC Protocol). The IGSC goes further and requires all potential customers to be screened against the Office of Foreign Assets Control's Specially Designated Nationals List; the US State Department Debarred List; the Bureau of Industry and Security's Denied Persons List and Entity and Unverified Lists; the German HADDEX List; and any other applicable national/regional screening lists (s.2.2 IGSC Protocol). Potential customers whose orders are 'flagged up' during automated screening are then investigated further before a decision is made as to whether the order will be accepted, for both of the associations recognize that certain institutions require products that might be flagged during the automated screening process for legitimate purposes. The IGSC requires that companies maintain records of all sequence and customer screening results for a minimum of 8 years, as well as every product that the company has produced and delivered, for at least 8 years (s.3 IGSC Protocol). The IASB requires that records of all 'suspicious inquires and positive screening hits' to be maintained for at least 8 years, as

556 IASB (n 451).
557 IGSC (n 451).
558 Council Regulation (EC) No 428/2009 of 5 May 2009 on the setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items [2009] OJ L134/1

well as statistics on biosecurity and biosafety related inquiries and orders (the number of orders fulfilled/rejected etc.) for at least 8 years (s.4 IASB Code). The wording of each document is, of course, different, and the specific requirements may be slightly different, however the documents are substantively the same.[559]

4.4.2 Responses to the industry standards

Surprisingly perhaps, there has been very little response to the standards designed and implemented by the industry. However, the responses that have emerged, have been positive - 'The IASB has taken laudable first steps in providing government regulators with guidelines they can build from. Now the regulators need to act'.[560] This sentiment was reiterated by the industry itself. Stephen Maurer, an expert in law and public policy to co-authored the IASB Guidelines, commented during the standards war, 'I think if the government expressed an opinion, DNA2.0 would blink…' Maurer was and is right. In an article published by *Nature* representatives of DNA2.0 and Geneart (founders of the IGSC) wrote:

> 'Although we stand behind our self-imposed regulations, there is no doubt that government could act to improve its efficiency. For this reason, we call upon both the United States and Europe to require all makers of synthetic genes to screen according to a list of restricted sequences compiled by the relevant experts. We have done our best to craft a screening list, but we believe that our governments should be able to provide the most up-to-date and accurate list of restricted sequences.'[561]

The government in the USA did indeed act. In 2010, after 3 years of research and drafting,[562] the US Department of Health and Human Services (HSS) published the final version of their Screening Guidelines.[563] The guidelines puzzled industry and academic

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[559] Check Hayden (n 554); Fischer and Maurer (n 553); Stephen M Maurer, 'Taking Self-Governance Seriously: Synthetic Biology's Last, Best Chance to Improve Security' [2012] University of Califronia, Berkeley Goldman School of Public Policy Working Paper No. GSPP12-003 <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2183306> accessed 31 March 2015.

[560] Editorial, 'Pathways to Security' (2008) 455 Nature 432.

[561] Jeremy Minshull and Ralf Wagner, 'Preventing the Misuse of Gene Synthesis' (2009) 27 Nature Biotechnology 800.

[562] Heidi Ledford, 'Gene-Synthesis Rules Favour Convenience' (2010) 467 Nature News 898; Wadman (n 462).

[563] Department of Health and Human Services, 'Screening Framework Guidance for Providers of Synthetic Double - Stranded DNA' (2013) <http://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf> accessed 31 March 2015.

experts:[564] Firstly, it was unclear why the government chose to draw up new guidelines, rather than simply endorsing one of the existing codes. Secondly, and following on from the first reason, the new guidelines are far less stringent in scope and application than either of the industry codes. Like the industry codes, the US government guidelines require both customer and sequence screening; the government guidelines are no more onerous than the industry standards, and in some respects, less so. Sequence screening, for example, is an automated process called 'Best Match'. Orders are screened against the Select Agents list and flagged up only if they are 'more closely related to the sequence of a Select Agent or Toxin (or Commerce Control List (CCL) item, when applicable) than to any other sequence in GenBank' (section 3).[565] 'Hits' (on either customer or sequence screening) are then subject to a follow-up screening, which requires verifying the legitimacy of customer/end user and the purpose of use.

This screening process does not go as far as either of the industry codes. Firstly, sequence screening is limited to the Select Agents list only meaning there is a there is a realistic possibility that some threats will go undetected, although the government claim that compiling a more comprehensive screening database is currently 'not currently feasible and hence is not provided in this Guidance'.[566] Secondly, the government protocols do not specify a *human* screening requirement in any part of the screening process, including the follow-up screen. Conducting a more thorough sequence or customer screen, and subjecting an order to human review are left to the discretion of each firm. These weaknesses are recognized by the government within the text of the guidelines; they write:

> '…the U.S. Government recognizes that there are concerns that synthetic dsDNA sequences not unique to Select Agents or Toxins or CCL items may also pose a biosecurity concern. The U.S. Government also recognizes that many providers have already instituted measures to address these concerns. The

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564 Stephen M Maurer and others, 'Making Commercial Biology Safer: What the Gene Synthesis Industry Has Learned about Screening Customers and Orders' [2009] Goldman School of Public Policy and Boalt Law School, University of California Working Paper <http://gspp.berkeley.edu/assets/uploads/page/Maurer_IASB_Screening.pdf> accessed 1 April 2015; Stephen M Maurer, 'End of the Beginning or Beginning of the End - Synthetic Biology's Stalled Security Agenda and the Prospects for Restarting It' (2010) 45 Valparaiso University Law Review 1387; Fischer and Maurer (n 553); Maurer (n 559); Sebastian von Engelhardt and Stephen Maurer, 'Industry Self-Governance and National Security: On the Private Control of Dual Use Technologies' [2013] UC Berkeley Goldman School of Public Policy Working Paper No. GSPP12-005 <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2189919> accessed 31 March 2015.

565 Department of Health and Human Services (n 563).

566 Ibid 9.

> on-going development of best practices in this area is commendable and encouraged…
>
> 'To this end, providers may also choose to use other screening approaches that they assess to be equivalent or superior to the "Best Match" approach or that supplement it…'[567]

Finally, the governmental guidelines are voluntary not mandatory.[568]

On the other hand, the government guidelines boast ease of implementation, efficiency and consistency. The protocols can be executed by a firm of any size, large or small, domestic or international, as screening is automated. The 'Best Match' methodology is based on responding to the binary question 'Is this sequence more closely related to a sequence from a Select Agent or Toxin (or a CCL item, for international orders) than to any other sequence?'[569] Thus, a 'hit' will be a 'hit' for all firms, offering consistency of standards. The narrow parameter of the question reduces the number of false positives.[570] Alternative methods, such as 'Top Homology' (here, all sequences that exceed a threshold level of homology to the make-up of an agent of concern are screened by humans) or screening against a customized sequence database, introduces arbitrariness into the process as the threshold for a threat to register may differ from firm to firm. Furthermore, involving human screeners in the process is expensive and introduces arbitrariness into the process. These arguments are not entirely compelling given the industry itself demonstrated a willingness to screen more widely, to employ human reviewers, and to make decisions vis-à-vis fulfilling an order.

In the accompanying FAQ's the US government provides some insight into its actions. In response to the question 'Why is guidance needed for dsDNA synthesis?' they write, 'Many synthetic dsDNA providers are eager for the U.S. government to provide them with guidance regarding best practices in mitigating biosecurity risks'.[571] In response to the question 'Why take a voluntary rather than a regulatory approach to screening synthetic dsDNA orders?' they point several reasons. Firstly, they applaud the

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567 Ibid 13.
568 U.S. Department of Health & Human Services; Assistant Secretary for Preparedness & Response, 'Frequently Asked Questions: Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA' (2010) <http://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/synbio-faq.pdf> accessed 31 March 2015.
569 Ibid.
570 Ibid.
571 Ibid.

industry's initiative 'The commercial DNA industry has acted responsibly in reaching out to the U.S. government to seek guidance'. Secondly, they point to a plethora of existing regulations that capture aspects of synthetic biology activity. Thirdly, they acknowledge the challenges synthetic biology presents for regulation, and the need to act carefully in order not to stifle innovation:

> 'Additionally, the field of synthetic genomics presents a novel challenge, and regulations may not provide the flexibility to address this challenge…
>
> 'Regulations take time to develop and may need to be modified to keep pace with science. The field of synthetic genomics is evolving very quickly. A voluntary approach is one way to deal with many uncertainties about the future of the field. Initial screening recommendations have been outlined in the document, but these may need to be adjusted in practice. The approaches taken in the document will be evaluated on an ongoing basis.'[572]

Finally, and most interestingly for the purposes of this chapter, they acknowledge the limited impact US regulations would have on the overall field: 'Voluntary guidance may provide a better opportunity to establish a baseline that is relevant internationally.'[573] In this aspect, the US government and I agree (see 4.5).

These answers in the 'FAQs' do not quite provide a wholly satisfactory explanation for the government's lack of appetite for regulation in the face of industry demand. Are they (the government) undermining the biosecurity threat posed by gene synthesis? Or is industry overestimating the scale and likelihood of these threats? By stepping back from regulation are the government showing their confidence in industry? Or is industry one-step ahead – responsible, engaged, pragmatic, and anxious to avoid the PR disaster (as well a financial destruction and set-back in scientific research) that would inevitably occur if they were linked to a bio-error, or worse an act of bioterror? In any event, the US government's Screening Framework falls far short of providing the type of guidance that industry hoped for, one is left with the impression that the guidelines were issued to placate the demand for regulation, rather than any desire to actually regulate. And yet, these protocols are more than any other government has provided.

I suggest, the need for thoughtful, targeted regulation persists. As the GPP story demonstrates, current 'hard' regulations do not comprehensively capture DNA design

[572] Ibid.
[573] Ibid.

work. This is not because DNA design has been carefully considered and deemed safe, but by chance – and what is also by chance is the fact that the GPP is relatively harmless. But, the field remains open for riskier projects to flourish. The need to manage these potential risks outweighs the attractiveness of simpler, 'light-touch' regulation such as that offered by the US government. In a field that is often characterized by uncertainties and risk this lowest-common-denominator approach tends towards heedlessness. Equally thoughtless are regimes that capture synthetic biology work wholesale through existing GMO laws (e.g. Europe), for this stifles scope for innovation, particularly in the world of underground science. A better approach would be careful consideration of the technology and the risks it poses resulting in regulations that oversee the field by assessing and targeting real risks with appropriate measures. I argue that this middle-ground approach can be achieved, in part, through RBR: the IASB and IGSC protocols provide a framework that can be expanded to fit this remit (see 4.5).

It is now nearly 5 years since the industry codes were published, and very little regulatory activity has occurred in the time that has passed. The IASB and IGSC protocols remain the most targeted and widely-adopted screening framework within the DNA synthesis field. Both the IASB and the IGSC remain active. The IASB code has been adopted by a number of companies around the world: ATG Biosynthetics, Biomax Informatics AG, Entelechon, Febit Synbio, PolyQuant, Shanghai Generay Biotech, Shanghai Shinegene Molecular Biotech, Inc. and Sloning Biotechnology.[574] The IGSC now has seven members who implement the protocols: Gen9, DNA2/0. Thermo Fisher Scientific, GenScript, Blue Heron, IDT, and SGI-DNA.[575] The IGSC claim that their membership represents approximately 80% of the gene synthesis industry.[576] Despite the fact that synthetic biology is a growing industry, and despite the occasional bouts of attention this field enjoys in the press, governments around the world have shown little appetite for regulation, neither individually nor collectively.

[574] 'Code of Conduct for Best Practices in Gene Synthesis - Current Undersigned' (*IASB*) <http://www.ia-sb.eu/go/synthetic-biology/synthetic-biology/code-of-conduct-for-best-practices-in-gene-synthesis/> accessed 1 April 2015.
[575] 'IGSC Members' (*IGSC*) <http://www.genesynthesisconsortium.org/members.php> accessed 1 April 2015.
[576] IGSC (n 555).

4.5 A risk-based approach

Governmental reluctance around the world to step in and regulate gene-synthesis has left the industry at liberty to write its own rules – and it has. In this section I argue that analysis of these industry codes reveals that they in fact typify a risk-based approach to regulation and further, that risk-based regulation is apposite for this part of the synthetic biology field. I further argue that the industry groups themselves are best placed to lead regulation in this field. This section begins with a brief explanation of what is meant by the term 'risk-based' regulation, its advantages and challenges.

4.5.1 What is 'risk-based regulation'? [577]

The concept of 'risk' can play many roles within regulation.[578] The term 'risk-based regulation' has two distinct, although often conflated, meanings:

> 'The first refers to the regulation of risks to society: risks to health, safety, the environment, or less usually, financial well-being…In this respect 'risk-based' regulation refers to the management of societal risk. The second, emergent meaning of risk-based regulation refers to regulatory or institutional risk: risk to the agency itself that it will not achieve its objectives. For regulators, in this newer sense, risk-based regulation involves the development of decision-making frameworks and procedures to prioritise regulatory activities and the deployment of resources organized around an assessment of the risks that regulated firms pose to the regulator's objectives…'[579]

Here, both definitions are relevant. Managing the societal risks of synthetic biology is the *raison d'être* of the regulations encouraged herein (see 4.1.1). However, we are equally concerned with the establishment of appropriate regulators and regulatory framework. In this instance, I propose a non-State agent – a knowledgeable regulator[580] – namely, the IASB or IGSC that must go further to demonstrate the legitimacy of its regulatory decisions. I argue that the transparency and logic of RBR can help do so.

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[577] See 1.2.5

[578] Black, 'The Role of Risk in Regulatory Processes' (n 57).
Black explains that the concept of 'risk' can be understood as playing four main roles in regulation: 1) it provides an object of regulation, 2) it justifies regulation, 3) it constitutes and frames regulatory organisations and procedures, and 4) it frames accountability relationships.

[579] Ibid 330.

[580] Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52).

Risk-based regulation is one of a number of regulatory approaches, mechanisms and procedures termed 'new governance'.[581] The antithesis to traditional, 'command and control' (CAC)[582] regulation, new governance techniques are generally characterized as responsive, flexible, reflexive, decentred, open to enrolling non-State actors in the role of regulator, and unafraid of confronting complexity.[583] These are all characteristics that are highly valuable in the context of DNA synthesis regulation due to it's fast pace, popularity amongst 'outside-establishment' parties, high-low risk-profile, and the fact that it is still a 'new' field.

RBR[584] is currently practiced by a plethora of regulators, from the Financial Services Authority (FSA) to the Human Fertilisation and Embryology Authority (HFEA).[585] Like other techniques of new governance,[586] the financial services sector, and in particular the FSA has contributed to the development of RBR.[587] It was cited as a good example of RBR in the Hampton Report,[588] enjoyed a relatively pleasant reputation until the banking crisis of 2007-2009. Regulation itself was not the only factor that led to banking crisis, but regulators were called to account for their role in the disaster; RBR together with other new governance methods took a battering.[589] Critique of the financial services regulatory regime does not necessarily sound the death knell for RBR or new governance; rather lessons can be learned to better implement these techniques.[590] Weakness identified within the financial services RBR framework need not transplant into the field of synthetic biology.

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581 See further: de Búrca and Scott (n 262); Scott and Trubek (n 9); Scott, 'Regulation in the Age of Governance' (n 9); Trubek and Trubek (n 8); Trubek and Trubek (n 9); De Burca (n 9); Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Ford, 'New Governance in the Teeth of Human Frailty' (n 262); Lobel, 'Renew Deal' (n 9); Lobel, 'Setting the Agenda for New Governance Research' (n 113); Sabel and Zeitlin (n 9); Black, 'Paradoxes and Failures' (n 40); De Búrca (n 262); Armstrong and Kilpatrick (n 262); Eberlein and Kerwer (n 262). See also 1.2.1. And, see chapter III for a parallel argument in favour of another new mechanism, polycentric principles-based regulation, for international stem cell research.

582 This refers to the classic model of regulatory influence: orders/standards/commands backed by (legal) sanctions. See further: Baldwin, Cave and Lodge (n 3) 106–7.

583 Black, 'Paradoxes and Failures' (n 40).

584 On the historical emergence of RBR see sections 1.2.2, 1.2.5 and: Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57); Hutter, *The Attractions of Risk-Based Regulation* (n 57).

585 HFEA Business Plan 2004-5 (London, 2005) For further examples of RBR in practice in the UK see: Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).

586 For example, principles-based regulation (PBR), see: Black, Hopper and Band (n 40).

587 Black, 'Paradoxes and Failures' (n 40).

588 Hampton (n 22). See also: 1.2.2

589 Black, 'Paradoxes and Failures' (n 40).

590 Ibid. In the context of principles-based regulation for stem cell research see: Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52).

As an organizational/procedural methodology, 'in its idealized form, RBR offers an evidence-based means of targeting the use of resources and prioritizing attention to the highest risks in accordance with a transparent, system and defensible framework,'[591] write Black and Baldwin summing up the sentiment behind RBR. How does this translate in practice? Foremost, RBR frameworks compel the regulator – here, I suggest, the IASB or IGSC – to focus on risks (what are they? which risks are riskier? which ones can be tolerated? which ones should be prioritised?) and selection, rather than rules-to-be-enforced. Of course, regulatory frameworks that are not proclaimed as RBR demand the same selection decisions of regulators, however RBR frameworks differ in that they 'render the fact of selection explicit and provide a framework of analysis in which they can be made'.[592] Whereas, in RBR risk-selection and decision making are in the spotlight, traditional regulatory frameworks cast the role of regulator as a 'rule-maker/enforcer' burying the selection process – for not all rules can be enforced in all firms at once – out of sight.

Operating RBR frameworks share a number of common elements, as identified by Black and Baldwin.[593] Firstly, these frameworks should identify the risks that threaten regulatory objectives. Secondly, they should establish the regulators 'risk appetite', that is to say, the type and level of risks that will be identified, tolerated and prioritized for regulatory attention. This can be tricky, and is often, ultimately determined by politics – what risks are seen as risks *and* acceptable to government, the public, and the media?[594] Thirdly, RBR frameworks incorporate assessing the likelihood of both inherent risks (those that are inherent to the activity being regulated) and management and control risks (the impact that management and control may have on increasing/decreasing the likelihood of inherent risks occurring) transpiring. Fourthly, regulators evaluate regulatees by assigning a score or rank, representative of their assessments. This can be expressed numerically or by category, in varying amounts of detail. Fifthly and finally, RBR frameworks allocate regulatory attention and resources according to risk evaluation, in other words applying the 'resources follow risks' mantra.

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[591] Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57).
[592] Ibid.
[593] Ibid.
[594] See also 5.3.6

As can be seen from this quick exposition of the formal elements of RBR,[595] the methodology lends an image of rationality, objectivity and calculation to the messy business of regulating. But, as Black and Baldwin point out, 'risk-based frameworks are not neutral, technical instruments. Each aspect of a risk-based framework involves a complex set of choices'.[596] At stake is the management of risks, resources and reputations; each element is individually challenging, and together, these three elements form a complex challenge of balancing interests and managing conflicts and tensions.[597] Furthermore, an RBR framework demands management of the internal focus (the systemic management of risks vis-à-vis the regulatory subject) and the external focus (managing the reputation and legitimacy of the regulator itself).[598]

There are good reasons to adopt a risk-based approach, but equally there are challenges to overcome; these factors will be briefly examined next in the context of gene synthesis screening.

4.5.2 Advantages and disadvantages of RBR

Why might a regulator opt for RBR? Black identifies five main reasons:[599] First, RBR might be adopted in order to improve regulatory function by employing a method of more careful allocation of scarce resources. Applying the 'resources follow risks' principle, regulators improve compliance by focussing their efforts on high-risk or maverick firms. This principle also enables regulators to act more consistently across a wide field, and in turn gives them a more panoramic perspective of risks across the field. Secondly, and following on from the last point, adopting RBR offers a consistent method of resource allocation for firms internally and those engaged in regulatory oversight of firms (this may be central government, or a private watchdog). Hence, RBR speaks to the high- and low-risk composition of the DNA synthesis – some sequences are dangerous, others not; some customers pose risks, others not. It also acknowledges the breadth of the field – not every instance of DNA design work can be monitored, however orders for gene sequences can be scrutinized for risk, and DNA design work regulated thus.

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595 See further 1.2.5
596 Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57) 185.
597 Black, 'Paradoxes and Failures' (n 40) 1053.
598 Ibid.
599 Black, 'The Role of Risk in Regulatory Processes' (n 57).

Third, RBR may be adopted in order to better respond to environmental changes (in the broader sense) within the field of operation. RBR operators are given the flexibility to identify, assess and prioritise risks in the field, and respond appropriately, on an on-going basis. Thus, the risks, the priority list, and indeed the responses may change as necessary in order to remain relevant to the field of operation. This level of flexibility is particularly important in a developing and fast-paced field such as synthetic biology; it allows regulators to step in time with advances in science and respond to changes in the political, social and economic spheres vis-à-vis gene synthesis.[600]

Fourthly, RBR might be introduced in response to previous regulatory failings.[601] The political rhetoric of RBR, as with new governance ideology and techniques generally, is pretty powerful; adopting RBR is seen as evidence of modernization, relevance and 'better regulation'.[602] These factors help legitimize the regulator to their regulatees, government/oversight, the public and the press. Regulating DNA synthesis is, of course, a brand new task – there is no history of failure – however, the rhetoric of RBR is still compelling. Establishing legitimacy and demonstrating relevance will be particularly important for the proposed regulator (IASB/IGSC) given it is a non-State agency comprised of those who would traditionally be seen as 'regulatees' (discussed further below). Fifth and finally, and RBR is a particularly efficient way of regulating, and this, following the regulatory burden and practices of the 1980's/1990's is compelling.[603] This factor too is pertinent to the regulation of DNA synthesis as the activity and risks vary greatly (e.g. from developing glowing plants to creating an artificial bacterium) and the population involved in the activity is dispersed, unidentifiable and indeterminate, necessitating an efficient method of regulating such a diverse field.

However, RBR is not without its own set of challenges. Firstly, asking regulators to identify and evaluate risks is not a technical, objective process but an exercise in judgment and discretion – and people can err.[604] In deciding which risks and which

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600 See chapter III and 5.2.2
601 Here, the context in which RBR emerged is relevant; see 1.2.5
602 Hampton (n 22); HM Treasury, Better Regulation Executive and Cabinet Office (n 23); Better Regulation Task Force, 'Principles of Good Regulation' (n 14); Better Regulation Task Force, 'Better Regulation - from Design to Delivery' (n 14); OECD (n 14); 'The Five Principles of Good Regulation' (n 14); 'Better Regulation' (n 14). See also 1.2.2, 1.2.5
603 Hutter, *The Attractions of Risk-Based Regulation* (n 57).
604 Baldwin, Cave and Lodge (n 3).

firms to focus on, the regulator is susceptible to making Type I or Type II errors, and therefore over- or under-regulating respectively.[605] RBR frameworks also focus regulators' attention on identifying individual sites of risk, at the expense of (rather, failing to identify) cumulative or systemic risks.[606] Secondly, resources do not necessarily follow risks in practice. Both Type I and Type II errors undermine the resource allocation argument of RBR. Even focussing on (correctly assessed) high-risk firms may be a displacement of resources as lower, multiple risks may be a greater overall risk, than a fewer number of high risks.[607] Thirdly, regulation is a politically sensitive activity. Regulators (State or non-State) require political support in order to operate fully and effectively.[608] And, the political climate will, to some extent, shape an RBR framework on paper and in practice. However, politics is a fickle game and when risks perceptions, tolerances and resource allocation decisions made by the regulator fall out of synch with the politics of the day it can cost the regulator both political support and their reputation.[609]

Fourthly, RBR frameworks provide little assistance when it comes to determining the level and type of regulatory intervention required. For this, regulators must look beyond the RBR discourse; here Black and Baldwin's argument for '*really responsive* risk-based regulation' can be helpful.[610] Really responsive regulation (RRR) is an approach in its

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[605] For example, the UK FSA tended towards Type II errors: Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).
[606] Baldwin, Cave and Lodge (n 3).
[607] Black and Baldwin, 'When Risk-Based Regulation Aims Low' (n 57).
[608] Black, 'The Role of Risk in Regulatory Processes' (n 57).
[609] Ibid; Black, 'Paradoxes and Failures' (n 40); Rothstein and others (n 68). The FSA learned this lesson in weeks and months following the peak of the banking crisis; 'light-touch' regulation fell swiftly from grace, as did the FSAs practices and reputation (see: Black, 'The Role of Risk in Regulatory Processes' (n 57); Black, 'Paradoxes and Failures' (n 40).). And see 5.3.6
[610] Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Baldwin and Black (n 81).
A historical note: really-responsive regulation a descendant of Ayres and Braithwaite's 'pyramid of enforcement' (see: Ayres and Braithwaite (n 82).). This set out a novel approach to the question of compliance, suggesting that regulators attune their response to firm non-compliance according to the gravity of the breach, (responses escalate from persuasion to punishment). A similar approach was suggested for industry-wide regulation in their 'pyramid of regulatory strategies' that offered range of strategies from self-regulation, escalating to command and control. Braithwaite later elaborated and extended the theory of responsiveness to apply beyond the beyond the context of enforcement (see: John Braithwaite, *Restorative Justice and Responsive Regulation* (Oxford University Press 2002); John Braithwaite, 'Responsive Regulation and Developing Economies' (2006) 34 World Development 884.)
Responsiveness within regulatory discourse has since become ubiquitous, forming a key role in shaping the subsequent regulatory trend of 'Smart Regulation' (see: Gunningham, Grabosky and Sinclair (n 27). and 1.2.3), which suggests using a multiplicity of regulatory instruments, and a multiplicity or regulators in a three-dimensional pyramid of smart regulation, and indeed, 'Better Regulation's' 'risk-based' approach. See: Hampton (n 22); HM Treasury, Better Regulation Executive and Cabinet Office (n 23). See also 1.2.2, 1.2.5

own right and not necessarily linked to RBR. It emphasizes applying any given regulatory strategy in a manner that is flexible and sensitive to:

1. the behaviours, attitudes and cultures of regulatees
2. the institutional setting of the regime
3. the different logics of regulatory tools and strategies, and how they interact
4. the regimes own performance
5. any changes in each of the foregoing elements[611]

Really responsive regulators are also cognizant of the varying challenges of implementing any given risk strategy. RRR provides a framework for practicing the flexibility and dynamism that RBR boasts in a nuanced, organized manner – in this sense the two frameworks resonate consonance.[612] Incorporating RRR into or alongside the RBR framework can also help mitigate some of the challenges of RBR noted in this section, such as failures/conflicts in risk detection and failures/conflicts in risk perception (see above), and inter-agency conflicts and 'model myopia' (see below). It also strengthens the development of a truly informed and knowledgeable regulator - and here certainly the IASB and IGSC boast an advantage over conventional regulators (see below) - which in turn can increase confidence in, and legitimacy of the regulator.

Fifthly, regulators operating RBR may find the logic and operation of their task in conflict with other regulatory agencies and approaches; this is particularly problematic for RBR given its claims of efficiency. Sixthly, RBR enables the regulator to establish a method of identifying and coping with risks, however, overtime the method may cease to operate optimally, failing to identify new risks and high-risk actors. RBR demands a certain level of continuous dynamism from its operators in order to avoid 'model myopia'.[613] Finally, in identifying and prioritizing risks, regulators essentially set out their own remit, defining the 'parameters of blame'[614] and scope of accountability, effectively insulating the regulator against liability for non-priority risks that may materialize on their watch. Although, perhaps the exposition of prioritization and

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Really-responsive regulation is a self-proclaimed relative of Selznick's broader conceptualization of 'responsiveness' (see: Baldwin and Black (n 81).) that demands the legal system ('regulator') to remain open to social knowledge and legitimate interests as well as its own logic.

611 Baldwin and Black (n 81); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57).

612 See 5.2.2

613 Baldwin, Cave and Lodge (n 3) 289.

614 Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57).

choice required within RBR systems enhances transparency - which is after all, a tenet of Better Regulation.[615]

These are all inherent challenges of RBR, not specific to its application within the gene synthesis industry. I argue that RBR is the best fit for the gene synthesis industry; the benefits (enumerated above) outweighing the challenges that must be overcome. Where DNA synthesis regulators operating an RBR system might need to exercise particular care is in managing the image and reputation of the field.

Poor PR might lead to a clash in risk perception and appetite between the regulator and government, the public and media (see further 5.3.6). This distracts from the task of regulating, as regulators become preoccupied with defending their own reputation and authority. At best, this defeats the efficiency-objective of RBR; at worst it can collapse the framework, resulting in a return to more familiar regulatory approaches and authorities, e.g. State-driven command and control, and restrictive regulations. However, I suggest that this will not be the fate of an RBR for gene synthesis. Anxious perhaps, to avoid a PR disaster similar to that of GM technology in Europe,[616] the synthetic biology field has done much to demonstrate openness and responsibility; for example, public engagement and implementing self-regulatory initiatives (i.e. IASB and IGSC).[617] This has established a relatively positive reputation for the field, which might help explain the nonchalance of governments around the world to issue regulations.

4.5.3 RBR and the gene-synthesis industry: uncovering a regulatory 'fit'

I argue that the IASB and IGSC provide a strong foundation for development of a fuller RBR framework. A cross-comparison of the protocols to the standard elements of RBR reveals that in many ways the protocols already conform to RBR. Considering sequence screening first: The screening database through which all orders are processed identifies sequences that are risky, these as we know, are those sequences identified on various government or government-endorsed lists. The programmed sequence filter

615 Better Regulation Task Force, 'Principles of Good Regulation' (n 14); 'The Five Principles of Good Regulation' (n 14). See 1.2.2

616 See: chapter II

617 Tait, 'Upstream Engagement and the Governance of Science' (n 491); Tait, 'Adaptive Governance of Synthetic Biology' (n 491); Tait, 'Governing Synthetic Biology' (n 491); Shukman (n 491); Henry I Miller, 'Will Overregulation In Europe Stymie Synthetic Biology?' (*Forbes*, 29 August 2012) <http://www.forbes.com/sites/henrymiller/2012/08/29/will-overregulation-in-europe-stymie-synthetic-biology/2/> accessed 1 April 2015.

documents the 'risk appetite'; sequence orders considered 'high-risk' are 'red flagged' for further attention, all other sequence orders are thus given an implicit 'low-risk' or 'no-risk' stamp and processed by the company without further investigation. Here, we see evidence of the first three features of a typical RBR framework: risks are identified, prioritized, and inherent risks assessed through the automated screening database. The human screening step of 'red flag' orders replicates these steps, and assesses the managerial and control risk of fulfilling a high-risk order. The outcome of this assessment is that either the order is processed or rejected. This is effectively the risk evaluation or score; implicit in the decision is an evaluation of the order in quantitative (inherent risk posed by the sequence ordered, determined through scientific evidence) and qualitative (the risk posed by the sequence *in the hands of this particular customer)* terms. At this point, the sequence screening and customer screening processes, which previously progress concurrently, merge.

The customer screening process reveals conformity to the elements of RBR as well: Minimum identification information is requested from all customers under both protocols, enabling risk management. At this stage the IGSC begins the risk management process; orders with a PO Box return address are rejected, and all potential customer are screened against various 'dangerous persons lists' to filter out high-risk customers. Acknowledging that certain addresses, entities and persons are potentially risker than others demonstrates risk identification, prioritization, and systematizing criteria to accept/reject the order demonstrates risk assessment and evaluation. Both protocols target customers seeking to order dangerous sequences for investigation (further identity checks and confirmation of legitimate end-use). Again, the IGSC provides specific details on their risk identification and prioritization criteria at this stage – 'IGSC companies supply genes from regulated pathogens only to researchers in government laboratories, universities, non-profit research institutions, or industrial laboratories demonstrably engaged in legitimate research' (s. 2.3 IGSC Protocol) – these entities are therefore considered lower risk than other potential customers (an independent garage-scientist for example).

The targeted customer investigation culminates in risk assessment and evaluation of the customer vis-à-vis the sequence ordered, and the stated purpose. The inherent risks are assessed (does this customer possess adequate research facilities and procedures to

maintain the security of the sequence? is the research purpose sound?), as are the managerial risks (qualitative assessment of management personnel and control processes). An evaluation is reached as to whether the customer order will be processed or not, representing the qualitative and quantitative judgments of the risk assessment, dovetailing with the evaluation stage of sequence screening. Although sequence and customer screening is set out separately in both protocols, as can be seen, there is necessary overlap at the assessment/evaluation stage, thus the outcome of the process will be a single decision (the order is either processed or rejected).

Record-keeping stipulations in both documents are consonant with the transparency-demands of RBR and can provide valuable data that will aid performance assessment of the regulator. Finally, in both documents the direction of resources is clear: time and expense is saved by automatically filtering all orders through a pre-programmed database, reserving costly and detailed investigation by human experts for orders flagged by the automated system as 'high-risk'. In short, resources follow the risks.

4.5.4 Adapting RBR for the gene synthesis industry

However, the screening protocols and the operational environment deviate from a standard RBR model as depicted in the literature in two aspects related to the character and identity of the regulator. Neither divergence, I submit, pose an insuperable barrier to operation of RBR in form or spirit. The RBR framework presented here is simply an adaption of the original model, adjusted to suit the specific context of operation.

First, the RBR literature drawn on here assumes two separate entities whose respective roles are clearly defined and demarcated: the regulator and the regulatee. However, in the instance of gene-synthesis regulation the role is conflated. Gene-synthesis companies both form 'the field' (those in the traditional 'regulatee' role) and perform regulatory functions of the protocols (fulfilling the 'regulator' role), which they themselves created. As part of 'the field' (which also includes the customer pool, researchers, investors and supporters), gene-synthesis companies are the subject or target of regulation; they can produce and sell sequences, some of which are potentially dangerous, and we (society, in the broadest sense) therefore prefer to monitor and control sales (what can be sold, who can sell it, who can buy it). Here, the companies themselves perform this task. Consider, for example, the evaluation stage of an order

for a regulated pathogen. The gene-synthesis company steps into the role of regulator, making the evaluation, and the customer, as the evaluatee/regulatee, awaits the outcome. And so, we arrive at a situation in which gene-synthesis companies play dual role of regulator/regulatee, to 'the fields' regulatee.[618]

Is this problematic? Not necessarily, I submit. Regulation is about the exertion of influence to shape behaviour in some way or other.[619] The body exerting influence might be the State, a State-mandated agency or non-State entity. However, the matter of who exerts influence in any given sphere of activity is important. Here, the entity acting as regulator comes from within the field, and is equipped with an in-depth technical knowledge of the activity (DNA synthesis) and possibilities, as well the politics of the field. They are uniquely placed to understand what is/is not important to scientists, what regulatory responses will be meaningful, what incentives and nudges[620] will be effective to lower risks and risky behaviour, and so on. Regulatory leadership by an organization from within the field might inspire confidence throughout the field in the protocols in a way that an external regulator cannot – this is one of the advantages of the *knowledgeable regulator*, and indeed self-regulation.[621]

This has been recognized by the US government who point out that, 'voluntary guidance may provide a better opportunity to establish a baseline that is relevant internationally.'[622] Voluntariness can encourage frank participation in the development process, which is valuable.[623] It also has another advantage over traditional regulatory processes; undertaking this task in the private sphere circumvented the lengthy and difficult process of attempting to achieve international government consensus. These factors may have eased the international launch of industry codes. Also helpful is the fact that the gene-synthesis community is internationally linked;[624] in drafting and launching the codes the IASB and IGSC were able to draw from, and deliver to, a pre-

[618] A similar argument is put forward in chapter III viz. regulating international stem cell research
[619] Baldwin, Cave and Lodge (n 3) chapters 2–3.
[620] This refers to the regulatory trend of 'nudge governance' whereby regulators use research from the field of behavioural sciences (e.g. behaviour patterns such as cognitive biases) to steer regulatee's towards making certain choices that will ultimately lead to fulfilling a particular regulatory aim. For a full explanation and analysis of nudge governance, including in the context of healthcare see: Quigley (n 385); Thaler and Sunstein (n 385); Sunstein and Thaler (n 385); Thaler, Sunstein and Balz (n 385).
[621] On the knowledgeable regulator see: Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52). Also see 5.3.3
[622] U.S. Department of Health & Human Services; Assistant Secretary for Preparedness & Response (n 568).
[623] See also chapter III
[624] Likewise, the international stem cell community (chapter III)

existing global network with whom they were already connected. Governmental institutions cannot boast the same level of industry confidence and connections. Therefore, the insight and outreach of the gene-synthesis companies is incredibly valuable, and properly utilized, can lend them the credibility, and political and public confidence to lead regulation in this field.

At present the IASB and IGSC enjoy the confidence of the wider field of DNA synthesis, US government, UNOG's BWC Implementation Support Unit,[625] and implicitly, the public (after all, we have not witnessed widespread public outcry or criticism in the press). However, I submit that both organisations need to go further in order to develop into truly legitimate regulators operating a robust RBR framework. The IASB describes itself as 'fostering international collaboration, both in the field of policy making and technical implementations to coordinate and harmonize policies and technical foundations'.[626] In developing their code, they included input from 'scientists, stakeholders, policy makers, social scientists and government bodies' however the same level of diversity is not evidenced on their membership list.[627]

Maintaining multi-disciplinary conversation and relationships is commendable; but including permanent multi-disciplinary representation within the Association transforms the regulator from a self-regulator[628] to a *knowledgeable* regulator.[629] The latter is far better equipped to defend itself against questions of accountability and legitimacy, and accusations of regulatory capture.[630] A regulator comprised of actors/groups with a stake in the development and future of DNA synthesis (in the context of gene-synthesis, this might include, for example: gene-synthesis companies, customers and researchers from the private and public sector, expert think-tanks, special interest/lobby groups etc.) will be necessarily engaged in a continuing discourse between parties

[625] Interview with Richard Lennane (Head) and Piers Millet (Deputy Head) of the Biological Weapons Convention Implementation Support Unit, United Nations Office for Disarmament Affairs, (Geneva, Switzerland 9 April 2013)
[626] 'Organisation Overview' (*IASB*) <http://www.ia-sb.eu/go/synthetic-biology/organization/overview/> accessed 31 March 2015.
[627] The IGSC boast no such multi-party, multi-disciplinary approach within their organizational literature although they 'welcome comments and suggestions to improve the Harmonized Screening Protocol from scientists, regulators and other interested parties' (IGSC (n 451). – *Revisions to the HSP*). The suggestions made here apply equally to the Consortium.
[628] For an overview of self-regulation, including its advantages and disadvantages please see: Baldwin, Cave and Lodge (n 3) Chapter 8; Black, 'Decentring Regulation' (n 333).
[629] Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52); Devaney, 'Regulate To Innovate' (n 52); Prosser (n 311). See chapter III, particularly 3.5.1
[630] Baldwin, Cave and Lodge (n 3) 43–5. See 3.5.1 and 5.4.1 on legitimacy and accountability

bearing divergent backgrounds, interests and perspectives. This consultative process builds in a layer of accountability (participating actors within the framework will hold each other to account), that legitimizes the choices and decisions of the regulator, both internally (within the field) and externally (to the public, the media etc.). Operated by a knowledgeable regulator, the internal discourse of the RBR framework will help the regulator to appreciate disjunctions of risk perception, realize conflicts between risks, and undertake sharper, more rounded performance assessments. It will also help the regulator to forecast risks, particularly new risks as they arise, and introduce a quality of dynamism that can help combat 'model myopia'. Under these conditions, the collapse of the regulator-regulatee distinction is not problematic. The perspicacity of the knowledgeable regulator can be strengthened by engaging in 'really-responsive' regulation, resulting in a heightened, prismatic awareness of the operational environment and therefore more nuanced regime. Incorporating multi-discourse into RBR comes at a cost; however, what is lost in time and efficiency is gained in a more informed and responsive regulator and regulatory framework.

The second deviation from the standard RBR model is that the role of regulator is not being fulfilled by the State or an agent of the State. This too, is unproblematic, for as noted earlier the State is not the only legitimate regulator in town. Governments (including their associated agencies) do not have sole jurisdiction over the task of regulating, and nor should they.[631] The discourse of 'new governance' tells us that the task of regulating ought to lie with the entity best suited to exert influence. I suggest the gene synthesis sector is in a strong position to design and implement informed regulations. Further, I suggest that the development of industry-led organisations into truly knowledgeable regulators will place them in an even stronger position to lead regulation in this field. The organisations have already demonstrated that they have the technical knowledge, capability and will to regulate the field of commercial gene-synthesis. Conversely, governments around the world have demonstrated little inclination to step up to the task. This may be evidence of genuine disinclination for the task, or perhaps a savvy move to co-opt private sector resources in order to fulfil the task.[632]

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631 See chapter III for a further example/argument of non-State regulation

632 Colin Scott, 'Gatekeeping and Non-State Intermediation in Regulatory Governance' in David Levi-Faur and Jacint Jordana (eds) (2005) <http://regulation.upf.edu/ecpr-05-papers/cscott.pdf> accessed 31 March 2015. 'Gatekeeping' is a concept that explains the public co-option of private resources to fulfill regulatory functions that would ordinarily fall to the state(s). Here the suggestion is one of *modified*

Nonetheless, political risk perceptions and preferences continue to inform the IASB and IGSC screening protocols, for these are imported into the framework via the various sequence and persons lists that orders are screened against. Both protocols pledge on-going review and updates, but this may not prepare them for radical and/or sudden shifts in the political risk appetite. At present, international risk appetites appear to be similar and stable, and both organisations have adopted a policy of constructing the screening database from as many relevant sources as possible. But if international political risk appetites diverge dramatically and this is reflected in the source material, or socio-political risk perceptions inflate, the organisations will be faced with a tough decision as to whose appetite to appease.[633]

So far, the industry protocols are working. No news of a synbio-error or act of synbio-terror has reached the newsstands (at the time of writing) indicating that members of the IASB and IGSC (the majority of the sector) are implementing the protocols with due care, and non-members are acting prudently. There are reasons as to why it is working. If a gene-synthesis company were to be linked to a bioerror or act of bioterror, the damage to reputation and impact on business would likely devastate the company in question. Furthermore, the loss of reputation would likely not be contained: the field as a whole would take a hit. Similarly, investors across the sector may become wary and withdraw support. Finally, such an event might stir governments to take action in the form of tougher, more restrictive and more burdensome regulations. All this, would impact the scientific and commercial trajectory of DNA design.

Yet there remains an elephant in the room. Although the protocols have been adopted and implemented (successfully so from all accounts) by the majority of the commercial gene-synthesis sector there is no mechanism of enforcement in place in the current framework. Any gene-synthesis company can adopt either of the codes – but how do we know that they are implementing the RBR framework robustly, if at all? Whilst the codes *are* voluntary, firms may adopt them for reasons other than the interests of regulation, such as bolstering reputation, or community pressure. Despite the self-

gatekeeping, as the task of regulating commercial gene-synthesis does inevitably fall to the state(s), indeed, the state(s) might not be the entity best suited to assume the regulatory role.

[633] See 5.3.6

interests of gene-synthesis companies to implement the protocols with due care, not all actors will be persuaded by the reasons for regulation cited above, and given the nature of risks associated with regulatory failure (bioerror, bioterror) some form audit and oversight is still desirable. This function could be performed by the IASB or IGSC (rather, a select committee from the organization) as a developed, composite and knowledgeable regulator. Alternatively, audit and oversight could be performed by an external third party such as the state(s) (this might take the form of an approved national/regional government body or agent or an international governmental organization), an appropriate non-governmental organization, or private-sector expert. (The latter method introduces an element of independent oversight, which might be desirable, however, the question of who might perform this function depends on locating a suitably qualified and willing party.) Scheduled inspections and random spot-checks are at the disposal of auditors. Introducing audit and oversight into the overall framework more clearly delineates the task of regulating access to sequences and regulating the sale of sequences. Of course, oversight itself might take the form of RBR, with gene-synthesis companies being identified and prioritized as the (potential) 'risk-subject' to be assessed and evaluated. However, elaborating on *that* framework further is beyond the scope of this chapter.

Weak implementation and supervision are among the reasons cited for the failure of the FSA's RBR regime. Recalling the collapse of the British bank, Northern Rock, Black comments: 'the risk based model simply was not followed, but no one outside the immediate circle of officials responsible for Northern Rock was aware of this deviation'.[634] Gene-synthesis regulators have the opportunity to avoid such failures by developing transparent channels of audit and oversight. I submit that this is imperative in order to maintain the legitimacy of the regulator.

In addition to poor supervision the FSA has been criticized for failing to correctly identify and prioritize risks (using incorrect indicators, for example), failing to respond to identified risks robustly and quickly enough, lacking the skills and confidence to analyse and challenge regulatees.[635] In applying the RBR model to gene-synthesis much can be done to avoid these failings. Developing a composite, knowledgeable regulator can help mitigate poor risk perception and disjuncture in risk perception, as well as

[634] Black, 'Paradoxes and Failures' (n 40) 1054.
[635] Ibid 1055.

failings due to lack of skill and insight. This in turn can impart confidence and authority both inwardly within the regime, and outward facing. Incorporating RRR into the RBR model can assist in developing a culture and framework of responsiveness. Ultimately, the success of an RBR framework will depend on the strength and convictions of the regulator to implement the system and respond as necessary. At present the gene synthesis field has several factors in its favour: a supportive (bordering on ambivalent) political climate, an internal willingness to regulate and be regulated, and the confidence to actually do so.

4.6 Conclusion and the future of gene synthesis regulation

This chapter has focussed on the regulation of DNA design, a sub-field of synthetic biology. DNA design is a relatively mature and accessible area of research within synthetic biology; it has a diverse, disparate and expanding population of researchers, ranging from academic researchers to garage biohackers, and is beginning to develop real-world applications. For these reasons, and due to the risks associated with DNA design, as well as gaps in the current applicable regulations, I have argued that it is timely and prudent to consider *targeted* regulation of this field.

The overarching aim of the regulatory framework proposed here is to target and mitigate the risks associated with DNA synthesis, whilst facilitating responsible scientific progress and discovery. I have suggested risk-based regulation as the appropriate strategy to achieve this objective.

Two soft-law documents play a key role in the development of the proposed framework: the IASB and IGSC screening protocols. Formulated and implemented by the gene synthesis community themselves in the absence of formally mandated regulations, these protocols fill a gap in web of regulations that governs DNA design work. I have shown here that the protocols unwittingly demonstrate many of the essential features of an RBR framework. However, I also argue that by purposefully developing the protocols as an RBR framework the regime can be expanded and strengthened to better meet the overarching regulatory aims.

Importantly, I recommend that the 'regulator' function remain with the gene synthesis industry. Seen as 'regulatees' within traditional regulatory frameworks, I argue that organisations such as the IASB and IGSC possess the knowledge and influence to effectively regulate the field – more so than any government or third party organization. Collapsing the regulator/regulatee distinction in this way is a departure from both traditional models of regulation (e.g. command and control) and models of RBR presented in the literature referenced. However, through exploring the intricacies of this collapse in the context of DNA synthesis, I have shown that it need not be problematic. Rather, a knowledgeable regulator from within the industry is, at present, best placed to develop and conduct regulation.

The development of glowing plants is only the tip of the beginning of what we can expect from synthetic biology. As the field of DNA design matures so too will the number of practitioners increase, and its applications multiply and gain in sophistication. And, so too will the risks associated with DNA design work expand and increase. Only through carefully targeted regulation can the risks of this biotechnology be contained in a way that does not stifle innovation. I argue that the model of RBR presented here best meets the foreseeable demands and challenges of regulating DNA synthesis.

CHAPTER V

What makes a facilitative governance framework? An analysis of key regulatory qualities and characteristics in the field of emerging biotechnologies.

5.1 Recapitulation

This thesis has examined the application of new governance techniques to the international regulation of emerging biotechnologies through three case studies in the fields of genetically modified organisms (GMOs), stem cell research and synthetic biology (chapters II, III and IV respectively). Articulating an argument for the qualitative relevance of new governance – namely, flexibility, reflexivity, nuance, open discourse, and participation – to these areas of biotechnology, this thesis has explored how soft-law, new governance techniques might be incorporated into the broader hard-law architecture of cross-border regulatory frameworks. Doing so, it is argued, will enable regulation to better reflect our changing states of knowledge (scientific and socio-ethical) of these emerging biotechnologies, and so facilitate responsible innovation. I begin this concluding chapter by briefly revisiting each case study, before discussing the overarching themes that have emerged in this thesis and putting forward my conclusions and recommendations.

5.1.1 Case study 1: European and international GMO regulation

The first case study (chapter II) focussed on the role of (bio)ethics in developing and operating regulatory frameworks for biotechnologies. Specifically, it explored the role of ethics at three stages within the regulatory process: designing a regulatory framework; engaging with changing states of knowledge throughout the operation of the regulatory regime; and assessing the operation and outcomes of a regime.

This chapter draws on the regulatory experiences of the Golden Rice Humanitarian Board (GRHB). Golden rice is a pro-vitamin A-enriched rice developed to combat vitamin A deficiency in developing world nations, particularly where rice is grown and eaten as a staple food.[636] Through the story of golden rice, I analysed the role, scope and influence of ethics within European and international GMO regulations.[637] I concluded that neither dimension, European or international, offers sufficient 'space' within the

[636] See 2.1.1
[637] See 2.3, 2.4

formalities of the regulatory framework for on-going, open, ethical discussion and reflection. In the context of regulating biotechnologies, failure to accommodate these discussions is a serious shortcoming. This is because the ethical perceptions of a technology – here, GMOs – can change as the technology itself, and our knowledge and understanding of it, develops. This in turn, can affect our assessment of the projected goals (what we want to achieve) and outcomes (what we are actually achieving) of the regulatory regime. To maintain a relevant regulatory regime, a degree of reflexivity and flexibility is essential.

Examining the journey of golden rice through European and international regulations, I concluded that these frameworks are not equipped to assess and act on the changing perception and role of GMOs in the global community.[638] Current assessments of the risks, and particularly the benefits of GMOs, are disregarded.[639] The benefits of golden rice are considerable: the product delivers vital pro-vitamin A to nutrient deficient populations in the developing world in an accessible format. As to the risks: years of GMO consumption have not yet yielded concrete evidence of harm to human health. The frameworks also disregard the broader ethical, social, economic and political ramifications of allowing or disallowing a GMO product. In the context of golden rice specifically, its availability will affect the health and nutrition, food security and economic stability of certain populations.[640]

Thus, the blunt, one-dimensional character of these frameworks is revealed. They fail to acknowledge the multiple and changing contemporary contexts in which regulation operates as well as the competing ethics that underlie GMOs.[641] They lack the capacity to reflect on their own goals and outcomes, to adapt to change, and to recognize the various stakeholder groups with an interest in the regulatory regime and their views (these groups are not limited to the regulatee). And, they do not facilitate innovation in the field of genetic modification. All this produces socio-ethically dissonant results. In response, I suggest re-modelling the frameworks to include formal space for ethics-focussed discussions.[642] Further, I suggest developing a multi-track regulatory process that is cognizant of the varying contexts in which these frameworks operate (the merits

[638] See 2.4
[639] See 2.2
[640] See 2.4
[641] See 2.4.2, 2.4.4
[642] See 2.5.2

of the particular GMO product, the populations it would affect, and so forth) in order to respond practically, to some degree, to the discussions.[643]

Chapter II evolved from the early discussions on the ethical approach to be taken in this thesis. I had not planned to write an extensive section on the role of ethics (that is to say, the role of ethics pre-law, within the operating regime, and reflecting on the regime), intending instead to keep the focus solely on the mechanics of regulation. Nor did I plan to write on GMOs - a biotechnology that has somewhat fallen out of fashion in the field of bioethics.[644] Yet, in writing and discussing the ethical background and approach to this thesis I was encouraged to explore more deeply the relationship between ethics and regulation. The story of golden rice provided the stimulus to explore this relationship through an engaging, real-time, narrative. Since writing this chapter the media spotlight briefly turned to GMOs: the intentional destruction of the golden rice crop field tests in the Philippines[645] revived interest in the GMO issue (and golden rice in particular) and brought fresh relevance to this part of my thesis.[646] That said, the focus of chapter II is not the GMO issue itself; rather the GMO issue is an example of the complex interface between ethics and regulation and the challenges therein.[647]

The weaknesses identified in the European/international GMO framework set the groundwork for the argument in favour of a change in regulatory style, namely, the shift towards new governance[648] that is subsequently developed through the case studies in chapters III and IV. In contrast to the stifling and stagnant European/international

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643 See 2.5.1

644 See 2.1.2. On the GMO debate generally see: 'Weighing the GMO Arguments: For' (n 156); 'Weighing the GMO Arguments: Against' (n 156); Food and Agriculture Organization of the United Nations (n 156). On the precautionary principle approach/debate generally see: Stirling (n 158); Fuller (n 158); Brown (n 158); Stilgoe (n 158); Bell (n 158).

645 McGrath (n 146).

646 'GM "Golden Rice" Opponents Wicked, Says Minister Owen Paterson' (n 147); Carter (n 147); Dominiczak and Hope (n 147). See also 2.1.1

647 See 1.3, 2.5.2, 5.2.4

648 Recall, the term 'new governance' refers to a particular set of the regulatory approaches, mechanisms and procedures e.g. principles-based regulation, risk-based regulation. These approaches are non-traditional in that they are most easily defined by what they are *not* – traditional, command and control style regulation. See 1.2.1 and: de Búrca and Scott (n 262); Scott and Trubek (n 9); Scott, 'Regulation in the Age of Governance' (n 9); Trubek and Trubek (n 8); Trubek and Trubek (n 9); De Burca (n 9); Ford, 'New Governance, Compliance, and Principles-Based Securities Regulation' (n 9); Ford, 'New Governance in the Teeth of Human Frailty' (n 262); Lobel, 'Renew Deal' (n 9); Lobel, 'Setting the Agenda for New Governance Research' (n 113); Sabel and Zeitlin (n 9); Black, 'Paradoxes and Failures' (n 40); De Búrca (n 262); Armstrong and Kilpatrick (n 262); Eberlein and Kerwer (n 262).

GMO regulatory regime,[649] the frameworks proposed in these chapters are designed using new governance techniques that boast all the qualities that the GMO framework lacks: flexibility, reflexivity, nuance, openness, and a capacity to facilitate scientific progress. As demonstrated in chapters III and IV, in the context of regulating biotechnologies these qualities are highly valuable, not least because they encourage discussion and reflection (ethical and otherwise) at every stage in the regulatory cycle.[650] Thus, the GMO case study in chapter II showcases the contrast in regulatory conditions and characteristics between a traditional framework and new governance frameworks that I analyse in the chapters III and IV.

5.1.2 Case studies 2 and 3: new governance and the regulation international stem cell research and commercial gene synthesis

In chapters III and IV I analyse the application of new governance techniques in two different fields of biotechnology: Chapter III sets out an argument in favour of adopting polycentric,[651] principles-based regulation[652] (PBR) for the international governance of stem cell research,[653] while chapter IV proposes the further development of a risk-based regulation[654] (RBR) framework for the international governance of commercial DNA synthesis (a subfield of synthetic biology).[655] The theory and modelling of PBR and RBR is drawn from Julia Black's work in these areas, including her work with Robert Baldwin. As such, both chapters reference an account of these mechanisms developed, applauded, disparaged and salvaged in the UK financial services sector. I argue that despite the loss of reputation that PBR and RBR have suffered in the wake of the recent global banking crisis[656] the mechanisms remain compelling and useful. I argue that, properly implemented, these mechanisms have the potential to

[649] Vogel and Lynch (n 188); Löfstedt and Vogel (n 188); Vogel, 'The Hare and the Tortoise Revisited' (n 188); Vogel, 'Ships Passing in the Night' (n 188); Vogel, 'The New Politics of Risk Regulation in Europe' (n 188).
[650] See: 1.2.1, 3.1, 3.2, 3.3, 4.1, 4.5
[651] Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332); Black, 'Decentring Regulation' (n 333).
[652] Black, Hopper and Band (n 40); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40).
[653] See 3.2, 3.3, 3,4
[654] Black, 'The Role of Risk in Regulatory Processes' (n 57); Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57); Black and Baldwin, 'When Risk-Based Regulation Aims Low' (n 57); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Black, 'Risk-Based Regulation: Choices, Practices and Lessons Being Learned' (n 57); Black, 'Paradoxes and Failures' (n 40).
[655] See 4.4.1, 4.5
[656] Black, 'Paradoxes and Failures' (n 40).

positively shape the future of biotechnologies in a way that is outside the capacity of traditional regulatory models.

The focus in both of these case studies is on the international dimension of regulation, reflecting the manner in which research and commerce is increasingly taking place. In Chapter III, the growing number of international stem cell research collaborations,[657] as well as related international policy and standard-setting collaborations, is highlighted.[658] In Chapter IV, I examine the global operation of commercial gene or DNA synthesis and development of competing international standards.[659] I focus attention on regulatory initiatives that the stem cell research community and gene synthesis industry themselves have developed and published in recent years, arguing that these initiatives are the ideal starting point for the development of new governance-based soft law frameworks to complement national and international hard law regulatory structures. These chapters explore how the insight and experience of those in the traditional 'regulatee' role can be harnessed through new governance techniques to develop nuanced and relevant regulatory frameworks.[660]

In chapter III I begin by explaining polycentric PBR and its application to the stem cell research field.[661] I argue the advantages of this approach versus a traditional command and control regime: primarily, principles (as opposed to rules) allow for flexibility as they can accommodate changing states of knowledge;[662] polycentricity, accommodates the myriad groups with an interest in the field beyond the traditional 'regulatee', thus delivering a regime that is capable of 'keeping up' with scientific advances and responding to the range of interests and concerns across the field (rather than simply those of the regulatee).[663] I further argue that a burgeoning polycentric PBR regime has begun to take shape. The latter can be evidenced through a number of voluntary international, interdisciplinary organizations that have produced codes of conduct and

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657 See 3.1
658 See 3.4 'Table D: International soft law instruments'
659 See 4.2, 4.3 'Table F: Non-legally binding regulations and guidance' 4.4 and specifically: IASB (n 451); IGSC (n 451).
660 See 3.4, 3.5, 4.4, 4.5.3, 4.5.4
661 See: Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332); Black, 'Decentring Regulation' (n 333); Black, Hopper and Band (n 40); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40). And sections 1.2.4, 3.2, 3.3
662 See 3.2
663 See 3.3

practice standards for researchers in the stem cell field.[664] I argue that these documents can be construed as principles, to be interpreted, applied and refined within the interdisciplinary, inter-party regulatory environment already formed through these organizations.[665]

Chapter IV focuses on regulating the commercial gene synthesis industry. Gene synthesis is a technique used for DNA design work, one of the more advanced niches within synthetic biology.[666] Gene synthesis is accessible and popular, engaging academic researchers as well as DIY/garage scientists resulting in a regulatory population that is difficult to identify and monitor.[667] For this reason, coupled with its risk profile (like many areas within synthetic biology, gene synthesis presents the 'dual-use dilemma'[668]), I argue that DNA synthesis demands regulatory attention and resources. Accordingly, a risk-based regulation method is recommended. RBR, readers will recall, provides a framework in which regulators can determine and assess risks, then decide upon which risks to focus regulatory resources.[669] RBR operates to target and manage deemed high-priority risks; low-priority risks are 'absorbed' within the system. This method of efficiently managing limited regulatory resources is particularly pertinent for DNA synthesis given the field is globally widespread amongst traceable and untraceable populations (i.e. DIY syn-biologists).[670]

As with the stem cell research field, the commercial gene synthesis industry has taken an active interest in regulatory matters. Drawing on interdisciplinary expertise from around the world, two competing international groups have formed and published protocols[671] for the industry in order to target and manage risk, which are currently being followed by companies. I argue that these protocols in fact closely mirror RBR, and that further developing and refining the protocols using this approach is apposite for the field.[672] In

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664 See 3.4 'Table D: International soft law instruments'
665 See 3.4
666 See 4.2.1
667 See 4.2.2, 4.2.3
668 This refers to the dilemma presented by a technology when it can be used for both benevolent and malevolent purposes. See: Garfinkel and others (n 483) 1.
669 See: Black, 'The Role of Risk in Regulatory Processes' (n 57); Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57); Black and Baldwin, 'When Risk-Based Regulation Aims Low' (n 57); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Black, 'Risk-Based Regulation: Choices, Practices and Lessons Being Learned' (n 57); Black, 'Paradoxes and Failures' (n 40). And see sections 1.2.5, 4.5.1, 4.5.2
670 See 4.2.2, 4.2.3
671 IASB (n 451); IGSC (n 451).
672 4.5.3, 4.5.4

chapter III, the sector-led initiatives were presented as soft, complementary frameworks to hard laws operated by formal regulators. Here, the nature and level of risk within this field creates a stronger argument for a closer relationship between the informal and formal regulators, and the frameworks that they operate, that might go beyond complementarity and result in formal endorsement or co-option of the protocols.

Chapter IV presents a further example of the applicability and relevance of new governance to the regulation of emerging biotechnologies. Alongside the study of GMO regulation (chapter II) it also serves as comparison case study in regulatory responses to technology, and the factors that shape these responses. The field of synthetic biology is in many ways a progression on genetic modification and the ethical debates surrounding both technologies prompt many similar concerns over the consequences of 'tinkering' with naturally occurring DNA patterns, resulting in comparisons between the two fields.[673] The poor reputation of GMOs in Europe and the strict, precautionary regime may well have served as a lesson to the scientific community in openness and engagement. Certainly, synthetic biologists have been eager to explain their work, enter debates, engage with the public, and take initiatives to act responsibly – as evidenced through the development of the screening protocols – in a manner unprecedented by the GMO community. Arguably, it is the contrast in behaviour and attitude that is responsible for the kinder public perception of synthetic biology, and not only the absence of *strict* regulations, but the absence of *any* targeted, formal regulation.

Formal regulations for synthetic biology may yet be necessary. If so, it is anticipated the relationships developed now through new governance strategies will be highly valuable: Those developing formal regulations will be able to take advantage of this network of relationships and pre-formed channels of communication between the scientific community as well as other stakeholders and interested parties (including regulators), as well any the soft law documents in operation. This will enable them to design regulations that better reflect and balance the positions of all parties across the field. These advantages were certainly not available to the architects of GMO regulations – which is perhaps reflected in the resulting regime(s).

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[673] Tait, 'Upstream Engagement and the Governance of Science' (n 491); Tait, 'Adaptive Governance of Synthetic Biology' (n 491); Tait, 'Governing Synthetic Biology' (n 491); Shukman (n 491); Miller (n 617). See also: chapter II

5.2 Key characteristics and qualities of facilitative frameworks for emerging biotechnologies

In each of the three case studies undertaken in this thesis I have focussed on the design and development of a regulatory framework specific to the area in question - GMOs, stem cell research and synthetic biology. However, through these case studies some general themes emerge.

Regulation is not a neutral tool; it can function to encourage or restrict scientific progress. The focus throughout this thesis has been on developing regulatory frameworks that operate to facilitate responsible scientific innovation and realize applicable benefits of biotechnology. The case studies undertaken here provide examples of contrasting regulatory function and effect. The first case study, on GMOs, is an example of a restrictive regulatory framework and its effects on the trajectory of technical progress and the sector's reputation. The latter two case studies, on stem cell research and synthetic biology, demonstrate how regulation might function to encourage innovation within a responsible framework. Through the three case studies some deductions can be made on the characteristics and qualities that are desirable for the construction of facilitative regulatory frameworks.[674] In this section (5.2) I go through these features as they arise within each case study, and state my final conclusions and recommendations below. The question of how to achieve these traits requires making choices between various regulatory 'settings': when to opt for hard or soft law;[675] which new governance technique to use; the jurisdictional dimension; and assigning roles within regulatory process. These matters too are discussed below (section 5.3).

5.2.1 Context

One of the key themes that emerge from this research is the importance of context.[676] Social (e.g. cultural, religious), economic and political contexts can sometimes help

[674] These deductions resonate with the 'regulatory desirables' identified by Farrell, Devaney, Hervey & Murphy: Farrell and others (n 122).
[675] See 1.4.2
[676] The importance of context 'in understanding the way in which regulation of specific health technologies emerges, persists, and changes over time' is also highlighted by Farrell, Devaney, Hervey & Murphy: Anne-Maree Farrell and others, 'Contextualising the Regulation of Health Technologies' (2012) 4 Law Innovation and Technology 113, 118.

explain regulatory frameworks;[677] I contend that it is equally important that regulation *is* in fact cognizant of context. In chapter II I considered the operation of international regulations for GMOs in light of changing and varying geo-political environments around the world.[678] Here, the context in which the regulatory subject – GMOs – exists is central to its purpose and use, and therefore the regulatory objectives. This case study demonstrates the consequences of failing to fully appreciate context(s) of operation as they develop and change – the result is an incongruous and out-of-date regulatory framework that stifles progress and the development of applications.[679]

Chapter III considered the international regulation of stem cell research, teasing out factors that distinguish this field from other areas of biotechnology. These were identified as the increasingly collaborative nature of research across national borders; the fast pace of scientific advances in the field; the technical complexity of the regulatory subject matter; the competing ethical positions that underlie research in this field; the limited and traceable research population (traditional regulatees); and the myriad groups with a vested interest in the future of stem cell research. Likewise, in chapter IV I draw out factors that distinguish the operation of commercial gene synthesis. These are the risks associated with gene synthesis (in particular, dual-use); the ease of access to this technology; the untraceable, as well as traceable, user populations (traditional regulatees); the international platform for gene synthesis work in both formal institutions and informal; DIY syn-biology/garage science forums; the technical complexity of the regulatory subject matter; the competing ethical positions that underlie research in this field and the fast pace of scientific advances in the field. I argue that these distinguishing features ought to inform the design of specific regulations in each field in order to avoid the inertia plaguing the GM sector and enable science to progress responsibly and deliver applications.

Understanding the specific context in which the regulatory subject operates and is perceived, as well as the individuals, groups and institutions involved in, or with an interest in, the regulatory subject matter (the 'regulatory population') is crucial to the design and implementation of an appropriately tuned regulatory system that motivates

[677] Ibid 118–21.
[678] See 2.4.4
[679] See 2.4

compliance.[680] Contextual understandings can inform both the form and content of regulation. The latter is obvious, the former, perhaps less so, and I discuss the relationship between context and determining regulatory form and mechanisms in detail further below.

5.2.2 Adaptability

Throughout all three case studies I have argued that adaptability should be a key feature of the regulatory frameworks for biotechnologies. This is essential in order for the regulatory framework to remain up-to-date with both the science itself and our ethical understandings of the science in question. Inherently adaptable approaches such as PBR or RBR are better equipped to keep a-pace with biotechnology (i.e. principles can adapt, and risk assessments adjust, as the technology develops) compared to traditional legislative and juridical processes of regulation, which are significantly slower and more time-consuming.[681] An example of the latter is seen in chapter II where the lack of flexibility within European and international GMO regulatory frameworks and out-dated understandings of the biotechnology itself is critiqued. In order to avoid similar stagnation in other areas of biotechnology – particularly those enjoying a rapid pace of progress – adaptable regulatory mechanisms are recommended. Thus, in chapter III I propose the development of a polycentric PBR regime for stem cell research, emphasizing the flexibility of principles over rules. Likewise, in chapter IV I propose the development of a risk-based regulation framework for commercial gene synthesis, highlighting the adaptability afforded to regulators to determine and manage risk.[682]

5.2.3 Reflexivity

Reflexivity[683] goes hand in hand with adaptability: unless there is 'space' for, and procedures that encourage self-reflection, a framework will find it difficult to adjust itself to internal and external factors. The absence of space within the GMO regime for actively reflecting on regulatory aims and impacts – particularly *a propos* ethics – is

[680] This is linked to the point made below (5.3.3) on the importance of the 'knowledgeable regulator'. On this point see: Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52).
[681] See 1.2.1, 1.2.4, 1.2.5, 3.2, 4.5
[682] On the choice of regulatory approach see 5.3.1
[683] Laurie, 'Reflexive Governance in Biobanking' (n 283); Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40); Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40).

critiqued in chapter II.[684] Learning from the history of GMO regulation, in chapters III and IV I explore how reflexivity can be achieved in the contexts of regulating stem cell research and gene synthesis.[685] Reflexivity is amongst the qualities that new governance boasts; thus, in chapter III I put forward a polycentric PBR regime for international stem cell research, and in chapter IV an RBR regime for international gene synthesis is proposed.

However, new governance mechanisms are not in themselves a magic wand that absolutely compels reflexivity, which is easier said than done. In her analysis of how new governance fared in the recent banking crisis, Black writes:

> 'If the financial crisis has a broader lesson for regulators elsewhere it is this: it is not enough to ask regulators or others to engage in self-critical learning, to assess whether they are performing their tasks well. It has to be asked whether they are performing the right tasks at all…'[686]

So, regulators of stem cell research and gene synthesis will need to be cognizant of how they function, a) internally, assessing *their* performance within the regime's own terms, and b) externally, assessing *the regimes* performance and function within the broader societal context. I have argued that the European and international GMO regimes fail the latter assessment. In order to not follow the same fate, regulators of the regimes proposed in chapters III and IV will need to be acutely aware of the *context* in which the regime operates (as discussed above, 5.2.1), self-assess internal and external performance (i.e. the reflexive process), and *adapt* the regime accordingly (also discussed above, 5.2.3). Reflexivity then, is a key process that connects contextual awareness and adaptability.

New governance structures can make it easier for those within the regulatory regime to engage in the reflexive process. In chapter III, the multi-party dialectic fostered through polycentric PBR encourages continual reflection and adjustment of international operational and ethical standards in stem cell research. In chapter IV, the interdisciplinary nature of the group(s) steering the international screening protocols promotes on-going discussion and consideration of appropriate risk management for gene synthesis. It is anticipated that these advantages, available through operating as a

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[684] See 1.3, 2.5.2
[685] See 3.2, 3.5, 4.5
[686] Black, 'Paradoxes and Failures' (n 40) 1062.

composite regulator within an international, interdisciplinary, multi-party regime, will go some way towards maintaining reflexivity within the regimes proposed in chapters III and IV. Furthermore, as these regimes strive to demonstrate legitimacy and accountability under the scrutiny of the public, the media and political system, the exercise of self/regime-assessment also engages the reflexive process.[687]

5.2.4 (Bio)ethics within regulation

Exploring and strengthening the relationship between (bio)ethics and regulation is an important theme within all three case studies.[688] It is explicitly analysed in chapter II, where I argue the importance of recognizing ethics within the regulatory process, from pre-law to the regulatory impact assessment stage.[689] In the GMO regulation case study, the absence of thought to the different contexts in which the international framework operates, and the wider impact of the European framework, is discussed in light of consequences for ethics.[690] Additionally, the failure of these frameworks to evolve as the technology evolves – and therefore its implications for various questions of ethics – is critiqued.[691] The frameworks proposed in chapters III and IV attempt to circumvent these shortcomings by emphasizing the importance of considering ethics within the regulatory process.[692] This is crucial for stem cell research and synthetic biology as both fields are still developing; as the science advances so too our understanding of the ethics underlying the science and its implications develop.

Throughout the three case studies the ethical context of the regulatory subject is highlighted.[693] Biotechnologies often provoke questions about sensitive and contentious matters and so warrant careful and continuous ethical consideration. Doing so maintains the regimes' relevancy, efficacy and legitimacy (discussed further below).

5.2.5 Calculating and managing risk

Determining and assigning risk is often an important consideration for emerging biotechnologies within regulatory discourse. Yet, risk management presents difficulties: we seldom know enough about the biotechnology in question, and its various

[687] See further 5.3.6, 5.4.1
[688] See 1.3
[689] See 2.5.2
[690] See 2.4.4
[691] See 2.5.2
[692] See 3.2, 3.3, 4.5
[693] See 1.3

manipulations, in order to accurately predict the full spectrum of risks (and benefits) at the regulatory design stage. Risk calculations can be made using a number of techniques: in this thesis, the GMO and gene synthesis case studies depict two contrasting risk-based approaches to regulation. In chapter II the precautionary approach[694] and its application to GMOs is analysed, and in chapter IV RBR[695] is recommended for the commercial gene synthesis industry. These case studies show how different risk management strategies can impact the trajectory of a field. The precautionary approach, weighted in favour of protective action, slows down progress as seen in the field of GMO research and development. I argue that RBR strikes a better balance between managing real risks and facilitating innovation by allowing the regulator to employ a specifically designed risk calculus, such as the two-step screening process developed in the international protocols for commercial gene synthesis.[696] This allows the regulator to take account of *context(s)* and *adapt* as required - meeting two key regulatory desirables.

The case study undertaken on stem cell research (chapter III) does not feature in this analysis on risk management. Risk is not a focus of that case study for two reasons: Firstly, risk management is not *as* pressing a concern in stem cell research (as it is in say, GMOs or synthetic biology) and in the interests of space, it is therefore omitted from discussion within this thesis. Secondly, the risks presented by stem cell research are different in nature to those presented by GMOs or synthetic biology. Namely, the risks associated with stem cell research are containable, whereas risks associated with GMOs and gene synthesis are not so. Focussing on the latter presented an interesting opportunity for comparing and contrasting risk management styles vis-à-vis a similar category of risks within the field emerging biotechnologies. This issue is discussed further in 5.3.1.

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694 See 2.2. Notable articulations of the principle include: 'Wingspread Conference on the Precautionary Principle: The Wingspread Consensus Statement on the Precautionary Principle' (n 161).; Rio Declaration on Environment and Development (n 160); Communication from the Commission on the Precautionary Principle (n 162); Cartagena Protocol (n 163)

695 See: Black, 'The Role of Risk in Regulatory Processes' (n 57); Black, 'The Emergence of Risk-Based Regulation and the New Public Risk Management in the United Kingdom' (n 57); Black and Baldwin, 'When Risk-Based Regulation Aims Low' (n 57); Black and Baldwin, 'Really Responsive Risk-Based Regulation' (n 57); Black, 'Risk-Based Regulation: Choices, Practices and Lessons Being Learned' (n 57); Black, 'Paradoxes and Failures' (n 40). Also see sections 1.2.5, 4.5.1, 4.5.2

696 IASB (n 451); IGSC (n 451). See 4.4.1, 4.5.3

5.3 Setting up the regulatory framework

5.3.1 Choosing the appropriate regulatory approach(es)

In this thesis I have discussed a number of new governance approaches, applying them to different areas of biotechnology research. An important theme that emerges then is the matter of choosing the appropriate new governance approach for each field. Here, I have recommended PBR for stem cell research and RBR for synthetic biology – why not vice versa? The question of determining the regulatory fit between the approach and the field comes down the character of the field to be regulated. Despite the bruises to its reputation following the banking crisis,[697] the spectrum of new governance techniques allow the 'regulator' great flexibility in deciding how much freedom, over what, and when, to give regulatees. New governance can form a restrictive or liberal framework depending on both the specific techniques utilized, and how they are implemented and enforced.[698] Careful choices must be made in ascertaining the nature of work undertaken in the field, maturity of the field, and the characters populating the field in order to employ the most appropriate technique. A brief comparison of stem cell research and synthetic biology reveals the different characteristics of each field.

Stem cell research is a relatively mature field of work (within the broad area of biotechnology); it has a longer history, our knowledge of the field is deeper and the research is beginning to demonstrate real benefits and applications.[699] Synthetic biology, on the other hand, is a far newer field that is still determining its own boundaries, capacity and definition.[700] The regulatory population in stem cell research is easily identifiable as the knowledge base, equipment and materials required to conduct stem cell research limits the work to certain institutions and organisations. In contrast, synthetic biology has a disparate regulatory population with research being conducted a

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697 Black, 'Paradoxes and Failures' (n 40).

698 See 1.3

699 See for example: Harwood (n 259); Hyder, 'Stem Cell Therapy for Autism Gets Clinical Trial Go-Ahead' (n 259); Hyder, 'Italian Government Orders Trial of Controversial Stem Cell Therapy' (n 259); Aitsi-Selmi (n 259); Young (n 259); Baker (n 259); Panizzo (n 259); Retassie (n 259); Paxman (n 259); Ilic (n 259); Steer (n 259); Tierney (n 259).

700 Editorial, 'Tribal Gathering' (n 446); 'Synthetic Biology: Beyond Divisions' (n 446); Collins and others (n 446); Scientific Committee on Health and Environmental Risks, Scientific Committee on Emerging and Newly Identified Health Risks and Scientific Committee on Consumer Safety, 'Preliminary Opinion on Synthetic Biology I: Definition' (2014) <http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_044.pdf> accessed 31 March 2015. Although note that some applications of synthetic biology have been realised, such as synthetic Artemesinin (Paddon and Keasling (n 470); Paddon and others (n 470). See further: 4.1.1

myriad of contexts from home garages (DIY synthetic biologists/biohackers[701]) to university research institutions and private companies; neither the research population nor their location(s) are easy to track. Importantly, the nature of risk that accompanies each field is very different: in stem cell research the harms are limited to the laboratory or medical setting, to individuals who conduct or partake in the research (e.g. clinicians, researchers and patients in a clinical trials). Thus, the risks are containable. In contrast, the risks that accompany synthetic biology are not easily containable: an accident in the laboratory (e.g. an escaped pathogen) or intentional misuse could lead to the devastation of entire environmental or mammalian living systems. Containable risks are no less serious than uncontainable risks, however they merit different regulatory or risk management.[702]

It may appear, trite to iterate but the differences in character of each field and the personalities that populate them necessitates the consideration of different regulatory approaches appropriate to each field of research. Hence, PBR, which offers researchers considerable freedom to develop their work, is argued as appropriate for stem cell research, a field that is established, identifiable, presents containable risks, and amenable to monitoring when necessary. Synthetic biology, which presents many inverse characteristics, and is currently in its experimental, developmental stage would arguably benefit more from RBR – i.e. focussing on resource allocation, risk identification and containment – than PBR. Adopting RBR for synthetic biology does not mean that researchers will not enjoy the flexibility to pursue goals as stem cell researchers operating within a PBR system would. Likewise, adopting PBR for stem cell research does not mean that risk management is neglected within the regime. Rather, choosing a particular regulatory method speaks to the regulatory priorities, which will differ from field to field, and as each field develops.

So, a field of research that is still in its early 'discovery' days, where the focus is gathering data and gaining understanding would benefit from a regulatory regime that promotes collaboration and sharing. Here, 'open source' models come to mind; the iGEM Registry of Standard Biological Parts[703] and BioBricks Foundation[704] are

[701] See 4.2.2
[702] See 5.2.5
[703] 'Registry of Standard Biological Parts' (n 505).
[704] 'The BioBrick™ Public Agreement' (n 505).

examples from the field of synthetic biology.[705] In contrast, a more mature field of research that has progressed to developing real-world applications might be more concerned with the production process, marketing and sales, and reception of the applications produced, than collaboration and sharing. These concerns would be reflected in the web of relevant regulations that apply to the field. In chapter III I have maintained that sharing data and collaborative research remain priorities for international stem cell research – hence the argument for internationally agreed operational standards.[706] However, as stem cell research advances from laboratory-based research to applications (a shift that we are only *just* beginning to witness now[707]) I suggest that regulatory priorities will change: clinical trials regulations, manufacturing standards, drug safety, marketing and sales approvals, and patent protection, may be amongst the regulatory concerns that will gain significance in the future.

5.3.2 Hard and/or soft law?[708]

There is another, broader question of regulatory choice, which goes beyond choosing between new governance methods, namely, when to opt for new governance (in the form of soft law, industry-led) and when to opt for traditional (in the form of hard law, government-led) methods of regulation.[709] Traditional, hard law frameworks govern both synthetic biology and stem cell research.[710] This thesis has examined soft regulatory options as *supplementary* to those hard law frameworks; importantly, the argument presented here is not that new governance should supplant traditional regulation, rather that it can provide complimentary structures for decision making and action planning. For, traditional regulation ('command and control') and new governance serve different very functions: in its simplest form, traditional CAC regulation issues strictures, whereas new governance offers methods and techniques to guide behaviour and arrive at mutual decisions.[711]

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[705] Bryn Nelson, 'Synthetic Biology: Cultural Divide' (2014) 509 Nature 152.
[706] See 3.1, 3.4
[707] Although note that there are a small number of clinical trials currently underway. See for example: Panizzo (n 259); Hyder, 'Stem Cell Therapy for Autism Gets Clinical Trial Go-Ahead' (n 259); Retassie (n 259); Paxman (n 259); Hyder, 'Italian Government Orders Trial of Controversial Stem Cell Therapy' (n 259); Harwood (n 259); Aitsi-Selmi (n 259); Young (n 259); Baker (n 259); Ilic (n 259); Steer (n 259); Tierney (n 259).
[708] See 1.4. 2
[709] On selecting mechanisms and approaches from the regulatory 'toolbox' see 'smart regulation' (1.2.3) and: Gunningham, Grabosky and Sinclair (n 27); Gunningham and Sinclair (n 29).
[710] See 3.1, 3.5.3 (on legally binding regulations); 4.3.1 'Table E: Legally binding regulations'
[711] Laurie, 'Reflexive Governance in Biobanking' (n 283); Laurie, 'Consent as Contract: What Does Solidarity Tell Us about the Evolving Nature of the Consent Process in Health-Related Research?' (n 283); Laurie and Sethi (n 284).

Thus, I argue, in chapter III that the international dimension of stem cell research would benefit from agreement on a number of operational matters, and further that this is best achieved through the dialectic process of polycentric PBR. The PBR framework would not interfere with national hard law regimes that govern stem cell research, rather it would operate as a complimentary system that offers the flexibility, reflexivity and so forth that an international CAC regime would struggle to attain. Likewise, in the field of synthetic biology, RBR offers a step-by-step decision-making tool to continually identify and assess risks posed by DNA synthesis, thereby filling a conspicuous regulatory gap in a far more efficient, effective and nuanced fashion than could be achieved through CAC. This is demonstrated through comparison with the case study on GMO regulation; the latter reveals a predominantly hard law framework (the Codex Alimentarius[712] is an exception) that lacks space and tools to debate, reflect, and reach decisions within the regime. Practical examples of the type of soft law frameworks in mind and their development process can be taken from the industry-led initiatives cited throughout this thesis: the Category A documents referenced in chapter III[713] and the two screening protocols discussed in chapter IV,[714] created by voluntary, international organisations within each respective field.

Regulatory goals can change over time as a field develops, as our understanding of the field develops, or as regulatory techniques develop. So, regulatory goals might shift, or we may find that a regime no longer serves its purpose.[715] All this is equally true of traditional regulation as it is of new governance. The latter, may enable the regulatory structure to hold its place a little longer as flexibility and reflexivity – hallmarks of new governance – enable a regime to 'travel' with the technology and reflect current understandings. However, as is anticipated for RBR in the context of DNA synthesis, over time, soft structures may evolve into hard laws by being co-opted by government(s) or acquire a firmer character through government endorsement.[716] Governmental co-option or endorsement is not at all necessary for a new governance-based framework to flourish and form a permanent part of the regulatory regime - new

712 See also 2.3.2
713 See 3.4 'Table D: International soft law instruments'
714 IASB (n 451); IGSC (n 451).
715 The UK's Human Fertilisation and Embryology Authority is an example of a regulator whose mandate has shifted over the years; most recently it acquired powers to license mitochondrial donation: Starr (n 2). See also 5.3.1
716 See 4.5.4 and Scott, 'Gatekeeping and Non-State Intermediation in Regulatory Governance' (n 632).

governance can succeed (or fail) on its own terms. If a new governance framework acquires a harder character, this demonstrates the transformative role that new governance can play in the development of regulation.[717]

5.3.3 Formal or informal regulator?

This discussion on the hard/soft law distinction leads to a related point on the distinction between formal and informal regulators. Whereas in chapter II a regime run by formally appointed regulators is distilled (again, the Codex Alimentarius is an exception to this), in chapters III and IV I suggest harnessing the knowledge and network of alternative parties as regulators ('informal regulators').[718] For, just as laws need not be 'hard' to have effect, regulators need not be 'formal' to have impact. In chapters III and IV I argue that these alternative organisations can sometimes perform the role of regulator in the field of biotechnology – moreover, they can perform the role better than those who may be formally appointed to do so.

In chapter III I identify a number or organisations that have developed regulatory guidance in the field of international stem cell research, such as the Hinxton Group, ISSCR, ISCBI, ISCF and WMA.[719] Chapter IV focuses on the work of two organisations, the IASB and the IGSC, who have developed regulatory protocols for international commercial gene synthesis.[720] Significantly, these organisations comprise or include those who would traditionally be playing the regulatee role - those engaged in the work (as well as advisors, experts and partners). The suggested shift from regulatee to regulator for these actors effectively blurs the distinction between two previously clear-cut roles. Collapsing the regulator-regulatee distinction as thoroughly as condoned in this thesis might be radical, however such a regulator, equipped with 'insider knowledge' of the field, has several advantages over traditional, formal, external regulators: a true understanding of the science and its possibilities and limitations; practical experience; a professional network. This, together with the know-how, experience and networks of other disciplinary experts (e.g. legal, ethical, economic) and stakeholders to be found within these organisations creates a powerful knowledge base

[717] See 1.4 on the relationship between law and new governance
[718] Otherwise termed 'knowledgeable regulators': Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52).
[719] See 3.4 'Table D: International soft law instruments'
[720] IASB (n 451); IGSC (n 451).

from which to operate. As a regulator, such an organization may be informal, but they are incredibly *knowledgeable*.[721]

Through their intimate knowledge of the field these organisations are in a position to know the type and style of regulation that would work well and that the field would respond to, what is important to the field, the capabilities and limitations of the field, what would be effective deterrents or 'nudges',[722] their capacity for compliance, and so forth. This insight is invaluable, allowing these organisations to regulate effectively and knowledgeably in a way that formally appointed regulators cannot easily achieve. Ultimately, capitalizing on the expertise and reach of these organisations as knowledgeable regulators paves the way for the development of meaningful, pertinent regulations – which, I posit, should be the goal of good regulation.

5.3.4 Regulatory enrolment

Unlike traditional CAC, new governance encourages participation from across the field.[723] Enrolling all those with a stake or interest in the regulatory subject, within the regulatory process, goes beyond the binary regulator-regulatee relationship that characterizes regulation in the traditional sense. I have elaborated above on the importance of appreciating context. Regulatory enrolment enables this through gathering perspectives within the field and encouraging inter-party engagement.[724] However, regulatory enrolment, as depicted in the case studies on stem cell research and gene synthesis, goes further than gathering information and points-of-view. New governance processes are discursive by nature and, properly applied, they can help absorb and translate these perspectives and inter-party discussions into a regulatory framework that reflects the shifting contexts of operation, helping to build and maintain a more informed, up-to-date regulatory framework. The enrolment of multiple parties

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[721] Devaney, 'Regulate To Innovate' (n 52); Devaney, *Stem Cell Research and the Collaborative Regulation of Innovation* (n 52).
Such a regulator might be vulnerable to regulatory capture (see: Baldwin, Cave and Lodge (n 3) 43–5.); however as I argue in 3.5.1 and 4.5.4 this avoidable. The international, interdisciplinary, multi-party structure of the PBR and RBR regimes proposed in this thesis draw into the regulatory process a multitude of perspectives that must be heard and taken account of. This together with the interpretative process of PBR, and consultative, reflective process of RBR can mitigate capture. See also: 5.4.1

[722] Quigley (n 385); Thaler and Sunstein (n 385); Sunstein and Thaler (n 385); Thaler, Sunstein and Balz (n 385).

[723] See 1.2.1 and Julia Black, 'Enrolling Actors in Regulatory Systems: Examples from UK Financial Services Regulation' (2003) 2003 Public law 63.

[724] See: Black, 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes' (n 332); Black, 'Decentring Regulation' (n 333). Also see 3.3

with different interests and stakes within the regulatory process can also help develop a more balanced regime through mutual critique and evaluation of biases.

Regulatory enrolment is a key feature of the proposals put forward in chapters III and IV: in chapter III, regulatory enrolment is encouraged through the polycentric element and number of interdisciplinary organisations engaged in the proposed framework,[725] and in chapter IV through the multidisciplinary organisations steering gene synthesis regulation.[726] Given that the impact of a regulatory framework can be felt outside the traditional regulator-regulatee relationship and outside its intended jurisdiction – this is exemplified in chapter II in the context of GMO regulation[727] – regulatory enrolment is important.

Finally, it is important to note that a new governance framework might at a later stage be formally or informally co-opted by government. If so, the government stands to inherit much, in addition to the regime itself: a knowledge base, pre-formed channels of communication and important relationships between stakeholders, which are less-easily formed in traditional regimes.[728]

The inclusion of those outside the traditional regulatory framework (e.g. interest groups, lobby groups, industry representatives, academia, indeed any party with an interest or stake in the regulatory process and outcomes), that comprised simply the regulator and regulatee, within the regulatory process, and the collapse of the traditional regulator-regulatee distinction, leads to an interesting question of who and what is shaping regulation. In the type of soft law, composite regimes envisioned here influences are numerous and varied, ideally leading to a collaborative regulatory regime, that is contextualized and cognizant of changing and competing interests. This style of regulation is a significant shift from the didactic character of traditional CAC.[729] However as I have demonstrated throughout this thesis there is much to be gained in moving away from traditional regulatory methods. Uncovering intricacies of power dispersion and influence within the nascent soft law frameworks depicted in chapters III

[725] See 3.3
[726] See 4.4
[727] See 2.4.4
[728] This point was made earlier in relation to synthetic biology: 5.1.2
[729] It must be noted here that the didactic character of CAC does come with one important advantage: *prima facie* legitimacy, via the democratic process. However, legitimacy can be attained and demonstrated in soft, new governance frameworks: 3.5.1, 4.5.4, 5.4.1

and IV remain outside the scope of this thesis; moreover, at present these frameworks are arguably not well established enough to benefit from such an analysis.

5.3.5 Jurisdictional dimensions

Linked to the issue of context is the matter of choosing the dimension(s) in which regulation is to operate; this should reflect and be appropriate to activity within the field. Although national regulations apply in each of the case studies in this thesis, the focus has been on the international dimension of regulation as this is the forum in which activity is increasingly taking place.[730]

5.3.6 Politics, the public and media influences

New governance or CAC, soft or hard, national or international, ultimately the determination of these regulatory settings will come down to political will and support. As seen in chapters III and IV, new governance thrived in the UK banking sector because it had, at least initially, political backing;[731] a supportive, but measured, political atmosphere will be needed if the frameworks proposed here for biotechnologies are to flourish. Media representations of the biotechnologies in question play an important role in shaping public opinion. Equally important are the biotechnology field's self-representations of their research. Examining the Jekyll-and-Hyde reputation of GMOs around the world (particularly the contrast between Europe and the USA[732]) and more recent comparisons between the reputations of GMOs and its trendier descendent, synthetic biology[733] (particularly in Europe), an open and publicly engaged sector can earn considerable public support and positive media. This plays a critical role in determining the type of regulation that finds political support.

730 See 2.3, 2.4, 2.5, 3.1, 3.4, 4.1, 4.3, 4.4, 4.5.3, 4.5.4

731 Black, 'Paradoxes and Failures' (n 40).

732 Vogel and Lynch (n 188); Löfstedt and Vogel (n 188); Vogel, 'The Hare and the Tortoise Revisited' (n 188); Vogel, 'Ships Passing in the Night' (n 188); Vogel, 'The New Politics of Risk Regulation in Europe' (n 188).

733 Tait, 'Upstream Engagement and the Governance of Science' (n 491); Tait, 'Adaptive Governance of Synthetic Biology' (n 491); Tait, 'Governing Synthetic Biology' (n 491); Shukman (n 491); Miller (n 617). And see chapter II

5.4 Challenges

5.4.1 Regulator legitimacy and accountability

Two main challenges encountered during the progression of this thesis are regulator legitimacy and regulator accountability. These matters are pre-emptively discussed during the thesis given that I advocate that an unofficially appointed body, including 'regulatees' assumes the role of regulator (particularly in chapters III and IV). It is trite to repeat that both legitimacy and accountability are essential aspects of a good regulatory regime.[734] In traditional regimes the electoral process and government administrative structure help achieve these qualities; in alternative regimes, such as those suggested here, regulator legitimacy and accountability is more difficult – though not impossible – to demonstrate.

In chapters III and IV I argue that certain informal organisations are in fact better placed to regulate on certain matters than formally appointed, traditional regulators, their legitimacy being demonstrated through the in-depth technical knowledge and experience of the machinations of the field that they possess.[735] Additionally, I argue that the new governance techniques advocated here can help develop legitimacy through encouraging inter-party engagement, open discourse and reflexivity. In chapter III, the multi-party communication urged through polycentricity means debate and discussion with a view to balancing interests are part of the regulatory process. So, although the regulator is not neutral and external, as a composite body with knowledge of the field from multiple perspectives it is not a biased self-serving entity. Similarly, in both chapters III and IV the interdisciplinary composition of the voluntary international organisations discussed also encourages deliberation and balance. Notably, in chapter IV, we saw that governments, through their marked apathy toward the task, have tacitly approved – even legitimized - the soft law frameworks that have emerged within the commercial gene synthesis industry.[736] Of course, all soft law frameworks operate on the basis of tacit government approval; governments, wielding the power of hard law can shut down a soft law regime if they so wish. In this sense, all soft law regimes are subject to formal oversight.

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[734] Baldwin, Cave and Lodge (n 3) 25–39.
[735] See 3.4 'Table D: International soft law instruments'; 4.3 'Table F: Non-legally binding regulations and guidance'
[736] See 4.2.2

So, regulatory legitimacy can be achieved through the regulator demonstrating knowledge and experience and the regime expressing qualities of openness, engagement, communicative interaction, reflexivity, flexibility and so forth – classic new governance qualities. Demonstrating regulatory accountability is a more complex task outside the established administrative hierarchies. In chapter III I argue that vibrant polycentricity and interdisciplinary engagement can go some way to achieving this; the argument being, parties will hold each other to account.[737] In chapter IV, maintaining the regime's reputation – a delicate matter given the controversial nature of synthetic biology – and responding to political and public risk perceptions adequately can develop confidence in accountability.[738] These defences to charges of missing accountability can be collectively summarized as contextual awareness and engagement – bringing this section full circle. There are also a number of simple, administrative steps an organization can take to aid accountability that are followed by formal regulators too: archiving communications, maintaining records of meeting minutes, open meetings, allowing public scrutiny of documents and records, and so forth.

However, demonstrating accountability, and indeed legitimacy, can be a more nuanced art. A regime that shows awareness of changing contexts, through its operation and responses to real-time events can be said to be achieving a kind of accountability. The omnipresent forces of public pressure and a watchful media are powerful incentives for a soft-law regime to mind its step, and guard its reputation. A regime that seeks to maintain its reputation is undoubtedly serving its own interests: a positive portrayal in the media can bolster public trust, keep the regime off the political reform agenda, and thus assure a position of regulatory authority. Conversely, a poor portrayal in the media can disintegrate public and political trust, leading to the swift loss of regulatory authority. I contend that this self-serving expression of accountability it is no less valuable than traditionally sought accountability. After all, the regime is being held accountable in a public forum that can be arguably harsher than traditional, formal channels of accountability. This subtle mode of accountability and legitimization can be particularly compelling for informal regimes of the sort proposed here, as they are all ultimately accountable to formal, governmental powers with the ability to shut down undesirable or failing regimes.

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[737] See 3.5.1
[738] See 4.5.4

5.5 Concluding Thoughts

Advances in science and technology have shaped life in the 21st Century, bringing ideas and inventions once thought the realm of pure imagination and science fiction, into everyday reality. From engineering agriculture to creating human life in a test tube, achievements in the field of biotechnology have contributed significantly to this phenomenon and there is every reason to believe that it will continue to do so. This thesis has explored how regulation can facilitate progress in emerging biotechnologies, specifically examining international activity in stem cell research and gene synthesis.

This thesis is propelled by two separate streams of discourse: firstly, the growing number of industry-led soft-law initiatives emerging in these fields, and secondly, the maturing of new governance within regulatory theory and practice. I have endeavoured to highlight the affinity between these two separate discourses. Serendipitously, the structure and development of these soft-law initiatives echo new governance-style arrangements and processes. And yet, emerging biotechnologies have much to gain in purposely reaching for the new governance tool-kit. The methods advocated here such as PBR and RBR are by now theoretically well-established, and come with valuable 'lessons learned' from practical experience[739] which provides regulatory designers with a conceptual framework that can be used to further develop these nascent soft-law initiatives. Furthermore, new governance encourages the development of certain qualities within the regulatory regime – adaptability, reflexivity, and a strong sense of context, communication and participation – that I have argued are highly desirable within regimes governing emerging biotechnologies. Indeed, I contend that these qualities are essential to the success of a regulatory framework that strives to facilitate research and development in the field of emerging biotechnologies.

Beyond setting up institutions and structures, and appointing personnel – practical matters – a number of elements need to be in place in order for any of the new governance approaches mentioned here to work. Trust between the various parties, groups and disciplines, a willingness to reach a set of workable regulations, open-mindedness, communication and understanding. As Black points out in relation to trust

[739] Black, 'Paradoxes and Failures' (n 40).

within PBR structures,[740] new governance can help develop these traits but they need to exist in the first place, at some level, in order to begin the process of developing a new governance framework. Fortuitously, establishing this base level of co-operation is less problematic for the emerging biotechnology fields discussed here (compared to say, the banking sector, analysed by Black[741]); I contend that the industry-led regulatory initiatives present evidence of the attitude and characteristics necessary for new governance to succeed.

The organic development of complementary soft laws by the international stem cell research and gene synthesis industries themselves discussed in this thesis indicate, I argue, a natural regulatory fit with new governance. In light of the analysis undertaken here, I submit that the best opportunities for responsible progress within the field of emerging biotechnologies lies in new governance.

[740] Black, 'Forms and Paradoxes of Principles-Based Regulation' (n 40).
[741] Ibid; Black, 'The Rise, Fall and Fate of Principles Based Regulation' (n 40); Black, 'Paradoxes and Failures' (n 40).

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