PROPORTIONATE AND ADAPTIVE GOVERNANCE OF INNOVATIVE TECHNOLOGIES:

THE ROLE OF REGULATIONS, GUIDELINES AND STANDARDS

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MAIN REPORT

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Executive Summary

Government financial support for the development of innovative technologies plays an important role in achieving the expected benefits from the UK's excellence in basic science. However, this support will fail to deliver the promised impact unless we can also develop smarter, more adaptive regulatory systems that are more proportionate to the levels of risk embedded in new technologies. This is particularly true of some of the technologies where the UK is identified as leading - life sciences, genomics and synthetic biology; regenerative medicine; financial technologies; and agri-science. Problems can arise because of inappropriate choice of a regulatory system to deal with new technologies and/or failure to adapt current regulatory systems to the needs of new technologies. There is a clear need to learn from past experience and to craft smarter regulatory systems that are able to incentivise innovation while still delivering safety, quality and efficacy.

These concerns about the fitness-for-purpose of our regulatory systems are leading to new emphases on adaptation and proportionality in regulatory regimes along with an 'innovation imperative' targeted to regulators. The premise of this report is that innovation would benefit from a formal consideration of the complementary roles that regulations, guidelines and standards could play in delivering the required proportionality and adaptation.

The project focused on where standards could contribute most effectively to different types of innovation (incremental or disruptive), across different industry sectors with differing experiences of regulation. The economic impact of standards would come from boosting productivity, opening up new markets, linking UK companies to global supply chains and reducing technical barriers to trade for incremental innovations; and supporting the development of more disruptive innovations. However, inappropriate, poorly specified or insufficiently adaptive standards can have negative impacts on the economic competitiveness of companies and countries and removing these disincentives is an important part of the overall picture.

General conclusions include the following: (i) current governance systems for innovative technologies lack coherence and are in need of a new approach to guide more effective decision making; (ii) where a regulatory system is imposed in the early stages of development of an innovative technology, it generally requires subsequent adaptation but proves difficult to adapt; (iii) exceeding the minimum requirements of a regulation ('gold plating') can have serious negative impacts on innovation; (iv) one benefit of standards is the reduction of variety, increasing the economic viability of markets, but for a disruptive innovation it may be more desirable to retain as much variety as possible until it becomes clear what the winning technology will be.

Choosing just a few important insights from each of the three case studies:

Personalised medicine manufacture for autologous cell therapies
In manufacturing, difficulties were experienced in adapting the chosen chemicals-based regulatory system to biological products and also in developing standards and guidelines for cell manufacture. For some clinical applications, there was no regulatory system in place. The competitive nature of the industry was leading to difficulty in persuading companies to collaborate and the resulting delays could cause risks to patients.

Industrial biotechnology/synthetic biology
Where environmental release of a GMO is involved, the existing EU regulatory system will require considerable adaptation if European economies are to be able to benefit from the use of the technology. Across all applications, standards are playing important roles in synthetic biology development, but in the 'contained use' manufacture of products using synthetic biology, regulatory adaptation is needed to make it easier to change the organisms used in the

manufacture of complex protein molecules when new more efficient processes become available. There is nervousness about political issues stemming from an association between synthetic biology and GM technologies and interviewees found it difficult to engage with regulators, unlike the situation in medicine-related sectors.

Financial technology (FinTech)

The regulatory systems in this sector are very different from the other two cases, the relevant risks being financial and reputational. More than in the other cases, regulators appreciated the potential economic and consumer benefits of FinTech and there were good interactions with innovators, particularly to support SMEs. There was a move away from detailed, prescriptive rules towards high-level, broadly stated principles to set the standards for regulated firms. Future standards will include the use of technology for automated risk assessment (RegTech) and a 'Regulatory Sandbox' approach is being developed to help new firms to navigate regulatory challenges. Regulators are also alert to the fact that big companies favour heavy regulation in that it acts as a barrier to entry for others.

Framework for proportionate and adaptive governance of innovative technologies

The report proposes a framework for conceptualizing the potential roles of standards, guidelines and regulations in the delivery of more proportionate and adaptive governance for innovative technologies, to support decisions by companies, regulators and policymakers.

In developing a regulatory system for a disruptive innovation with a novel value chain for which there is no existing regulatory precedent we have proposed a staged approach:

1. In the early stages of developing a technology, focus on PAS and/or consensus standards devised in collaboration with companies and scientists with expertise in the area;
2. As experience is gained and the future nature of innovative products and processes is clarified, adapt the initial standards and formalise them as guidelines that could then form the basis of a future regulatory system;
3. Based on these guidelines, in a more openly democratic process involving all interested stakeholders, develop legally binding regulations, couched in general terms relating to the desired outcome of the regulation; and
4. Also in an open democratic process involving all interested stakeholders, devise standards and guidelines to support compliance by those engaged in developing the new technology.

For incremental innovation that fits readily into existing industry value chains and current regulatory systems, the problem is more often that the regulatory system that has built up over a period of years is insufficiently adaptive to the needs of new technologies, and can unnecessarily inhibit innovation. Here standards can have an important role in enabling adaptation of the incumbent regulatory system so that it becomes more supportive of innovation.

Responsible Research and Innovation (RRI)

The report also proposes a more integrated approach to incorporating RRI (as desired by many stakeholders and citizens) within the overall approach to governance of innovative technologies. Current RRI approaches focus mainly on basic research, with the main emphasis being on stakeholder engagement, and they need to be extended to cover product and process innovation. There is a strong case for the BSI to support the development of a new standards-based approach to RRI *per se* and to extend this to developing standards for responsible behaviour by regulators/policy makers and by other stakeholders and citizens.

Acronym List

ACoP – Approved Code of Practice

API - Application Programming Interface

ATMP – Advanced Therapy Medicinal Product

BS – British Standards *(as in BS ISO 27001)*

BSI – British Standards Institution

CAT – Committee on Advanced Therapies (EMA Committee responsible for assessing the quality, safety and efficacy of ATMPs)

CEN – European Committee for Standardisation

CHMP – Committee for Medicinal Products for Human Use

CoP - Code of Practice (used in text separately from ACoP)

DD - Draft for Development

DFM – Design for Manufacture (standards)

DG – Directorate General (in the European Union)

DNA - Deoxyribonucleic Acid

EBE – European Biopharmaceutical Enterprises, trade agency representing biopharmaceutical companies

EDQM – European Directorate for the Quality of Medicines and Healthcare

EFSA – European Food Standards Agency

EMA – European Medicines Agency

ELSA – Ethical, Legal and Social Aspects (of scientific research)

EC – European Commission

EU – European Union

EY – Ernst & Young

FCA – Financial Conduct Authority

FDA – US Food and Drugs Administration

FinTech – Financial technology

FSA – Financial Services Authority

GCP – Good Clinical Practice

GILSP – Good Industrial Large Scale Practice

GLP – Good Laboratory Practice

GM – Genetic Modification

GMC – General Medical Council

GMO – Genetically Modified Organism

GMP – Good Manufacturing Practice

HMA – Heads of Medicines Agencies

HSE – UK Health and Safety Executive

ICH – International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICT – Information and Communications Technology

ISO – International Organisation for Standardisation

ISTR – Institute for Safety and Technology Research

ITF – Innovation Task Force (located in the EMA)

IVF – *In Vitro* Fertilisation

JMLSG - Joint Money Laundering Steering Group

JPAC – Joint Professional Advisory Committee

MAA – Marketing Authorisation Application

MEDDEV – Medical Device Guidance Documents

MHRA – Medicines & Healthcare products Regulatory Agency

MNC – Multinational Company

MSCs – Mesenchymal Stem Cells

NAS – US National Academy of Sciences

NGO – Non-Governmental Organisation

NIBSC – National Institute of Biological Standards and Control

NICE – National Institute for Health and Care Excellence

NIST – National Institute of Standards and Technology (US Department of Commerce)

OECD – Organisation for Economic Cooperation and Development

OFT – Office of Fair Trading

PAS – Publicly Available Specification

PR – Public Relations

PRA - Prudential Regulation Authority

PSR – Payment Services Regulator

QMS – Quality Management System

rDNA - Recombinant DNA

REACH – EU Registration, Evaluation, Authorisation and restriction of Chemicals Regulation.

RegTech – Regulations Technology

RI – Responsible Innovation

RIF – Responsible Innovation Framework

RMEG – Regenerative Medicine Expert Group

RNA – Ribonucleic Acid

RRI – Responsible Research and Innovation

SBLC – Synthetic Biology Leadership Council

SBOL – Synthetic Biology Open Language

SBSC – Synthetic Biology Standards Consortium

SME – Small and Medium Sized Enterprise

SNBTS – Scottish National Blood Transfusion Services

SWIFT – Society for Worldwide Interbank Financial Telecommunication

TSB – UK Technology Strategy Board

UK – United Kingdom

UN – United Nations

US / USA – United States of America

WHO – World Health Organisation

WIPO – World Intellectual Property Organisation

WTO – World Trade Organisation

1. Introduction

1.1 The concept of governance and its implications for advanced innovative technologies.

The concept of governance is complex and varies across fields of application, describing a process of exercising authority, the way that a city, company, or any organisation is controlled by the people who run it. Most definitions rest on three dimensions: authority, decision-making and accountability, determining who has power, who makes decisions, how other players make their voice heard and how account is rendered. The World Bank's World Wide Governance Indicators[1] include the above dimensions and envisage effective governance as incorporating a range of policy tools, including norms, standards and guidelines. The US National Academy of Sciences Report on Industrialisation of Biology (NAS, 2015, p. 20) describes governance as involving "… a variety of policy tools by which an industry's behaviour can be shaped, including education of industry actors, industry self-governance through standard setting, accreditation, government standard setting and regulation, public engagement and public scrutiny, tort liability, and other mechanisms for developing safety standards and controls".

The legislative element of a governance framework is based mainly on regulations and guidelines but can include standards, for example where adoption of a standard is accepted as evidence of compliance with a regulation. Running in parallel with the legislative system is a broad range of standards and industrial and societal norms, including: consensus standards developed by bodies like BSI and ISO; industry self-governance regimes involving standards and accreditation processes; government based advisory policies; education of scientists and industry actors; market-based networks; and engagement and dialogue processes to ensure conformity with societal goals and values.

In the UK and the EU there are concerns that the prevailing regulatory systems have become overly precautionary and disproportionate to the nature and extent of the risks presented by many technologies, and are hindering international competitiveness and the development of a vibrant economy (FDA, 2010; HMA, 2015; HM Treasury, 2015; Tait, 2007). This has led government bodies to refer to the EU Principle of Proportionality[2], for example as set out in 'Principles of Better Regulation'[3], including the following provisions:

- Only intervene when necessary.
- Remedies should be appropriate to the risk posed, and costs identified and minimised.
- Policy solutions must be proportionate to the perceived problem or risk and justify the compliance costs imposed – don't use a sledgehammer to crack a nut.
- All the options for achieving policy objectives must be considered – not just prescriptive regulation. Alternatives may be more effective and cheaper to apply.
- "Think small first". Regulation can have a disproportionate impact on small businesses.
- EC Directives should be transposed without 'gold plating' (the process where a basic EC Directive is given extra strength when incorporated into UK law).
- Enforcement regimes should be proportionate to the risk posed.
- Regulators should consider an empowering and educational, rather than a punitive approach where possible.

The language of proportionality is also echoed in a recent OECD Recommendation of the Council on Regulatory Policy and Governance (OECD, 2012):

[1] http://info.worldbank.org/governance/wgi/index.aspx#home
[2] http://eur-lex.europa.eu/summary/glossary/proportionality.html
[3] http://www.gov.scot/Topics/Business-Industry/support/better-regulation/5principlesofBetterRegulation

- Ex ante assessment policies should include a consideration of alternative ways of addressing the public policy objectives, including regulatory and non-regulatory alternatives to identify and select the most appropriate instrument, or mix of instruments to achieve policy goals. …. including complementary approaches such as through a combination of regulation, education and voluntary standards. The no-action option or baseline scenario should always be considered.
- Governments should avoid the duplication of efforts in regulatory activity in cases where recognition of existing regulations and standards would achieve the same public interest objective at lower costs.
- Regulatory governance is grounded in the principles of democratic governance and engages a wider domain of players including the legislature, the judiciary, sub-national and supranational levels of government and international standard setting activities, including those of the private sector, along with citizens and stakeholder groups.

1.2 Disruptive and incremental innovation

The concepts of disruptive and incremental innovation are increasingly discussed in the context of managing innovative technologies but often poorly defined. The relevance of these concepts in designing an appropriate governance framework is introduced here as a factor to be considered in decision making on the choice of standards, regulations and guidelines to be applied for innovative technologies. We define incremental and disruptive innovation as follows (Tait, 2007):

- **Incremental innovation** will fit well with the current business model of a firm, enabling it to continue to innovate around current business practices, generating competitive advantage relative to other companies in its sector through more efficient use of resources, or elimination of wasteful or environmentally damaging practices. It is less likely to generate stakeholder concerns, is more likely to have a pre-existing regulatory framework in place, but is much less likely to lead to sectoral transformations with significant commercial and societal benefits.
- **Disruptive innovation** involves discontinuities in innovation pathways, requires new areas of R&D, development of new markets and new modes of production, and (in some areas) potentially leads to stakeholder concerns at an early stage of development. Also for a disruptive innovation there may be no obvious regulatory precedent to govern potential human and environmental safety issues.

The governance framework in operation for an industry sector is increasingly recognised to have a significant impact on its capacity to innovate. For example, the more onerous, time consuming and expensive the regulatory system for an industry sector, the more it is dominated by the business models of large multinational companies and the more difficult it becomes for a small company with a disruptive innovation agenda to gain competitive advantage. Under these circumstances, small companies will engage almost exclusively in incremental innovation that is most likely to fit with the innovation strategies of incumbent multinationals, rather than aiming to compete with them on the basis of a disruptive innovation strategy (Tait, 2007).

The timescale and cost of the regulatory systems that prevail in the life science area partly explain the relative lack of disruptive innovation in life science related industries (Coombs and Hull, 1998; Tait, 2007; Tait *et al.*, 2007; Milne and Tait, 2009).

Achieving proportionality in governance systems will require adaptation of current regulatory regimes along with appropriate design of future regimes and the scale of the challenges will be greater for more disruptive innovation. The underlying premise of this report is that the facilitation of innovation, particularly disruptive innovation, has much to gain from a formal

consideration of the complementary roles that regulations, guidelines and standards can play in delivering the more proportionate governance approach needed to support commercialisation of basic scientific research.

The value of standards in supporting innovation (BSI, undated-a) lies partly in their diversity and ability to cope with a broad range of circumstances (e.g. covering products, processes, manufacturing and organisational behaviour); partly in their flexibility and adaptability to cope with rapidly changing understanding of opportunities and risks; partly in their ability to incorporate in their development the perspectives of a broad range of stakeholders; and also the fact that their use, although voluntary, is motivated by the desire of innovators to speed up and facilitate the path to commercial application.

This project considers the most important elements of the overall governance framework for innovative technologies in general and for three case study areas:

(i) Personalised medicine manufacture for autologous cell therapies;

(ii) Industrial biotechnology/synthetic biology; and

(iii) Financial technology (FinTech).

These case studies provide a useful range of challenges arising from both disruptive and incremental innovations.

- For the multinational companies (MNCs) in the pharmaceutical industry sector, **autologous cell therapies** are a disruptive innovation across the board, for manufacturing processes, value chains and distribution channels, target markets and reimbursement models. However they are much less disruptive for small and medium sized enterprises (SMEs) that have traditionally supported tissue transplants or for blood transfusion services (Tait, 2007; Mittra *et al.,* 2014b).
- In contrast, the use of **synthetic biology** in chemicals manufacture (industrial biotechnology), as currently being developed, is disruptive of manufacturing processes (requiring fermentation skills rather than the skills of the industrial chemist), but it will be less challenging for incumbent MNCs as the products envisaged do not disrupt current distribution channels or value chains.
- FinTech is an example of emerging technology that will be disruptive across the board for existing financial sectors, in R&D, product development and marketing stages. It will affect a wide range of financial services and products, as well as advisory and transaction platforms. However, the existing and future governance issues will be very different from those in the first two case studies and effectively governing this sector in a way that encourages innovation will be challenging.

1.3 Regulation/innovation interactions

This project explores the potential roles of regulations, guidelines and standards in unlocking successful innovation and accelerating technology commercialisation while continuing to ensure safety, quality and efficacy in products and processes. It will build on previous work of the BSI in this area (O'Sullivan & Brévignon-Dodin, 2012) and the workshops held in 2013 on the development of standards for synthetic biology to which the Innogen Institute contributed.

Research in the Innogen Institute since 2002 has made a major contribution to the increasing recognition that regulatory systems across the life sciences are having an inhibiting effect on innovation, beyond what is necessary to deliver safety, quality and efficacy (Bruce *et al.,* 2013; Courtney *et al.*, 2011; Mittra and Tait, 2012; Mittra *et al.*, 2014b; Tait *et al.,* 2007; Tait, 2009; Tait

and Barker, 2011), and current policy drives towards more proportionate regulatory systems have been able to build on these insights.

The following initiatives can be seen as moves in the direction of greater proportionality in regulatory regimes:

- strengthening the role of science (regulatory science) in delivering effective, proportionate regulation (US Food and Drugs Administration (FDA), 2010) and in development of the Accelerated Access Review[4];
- removing unnecessary regulatory restraints (UK Health and Safety Executive (HSE), 2014); and
- in the context of health-related innovation –
    - the US House of Representatives approved the 21st Century Cures Act to support the translation of discoveries into innovative therapies, including funding for the FDA to accelerate regulatory processes (Pharma Times, 2015);
    - the new European Heads of Medicines Agencies (HMA, 2015) strategy aims "to ensure that the European regulatory environment is one that facilitates the development of novel products as well as protects and promotes public health"; and
    - Sir Michael Rawlins has committed his tenure as Chair of the UK Medicines and Healthcare Products Regulatory Agency (MHRA) to speeding the approval of innovative medicines (Bryan, 2015).

This report considers the role of standards, as an integral part of a governance system, in contributing to regulatory adaptation and also in helping to avoid the problems that can arise where an ill-informed regulatory choice that is subsequently very difficult to reverse may be significantly hampering innovation (Tait, 2007; Mittra & Tait, 2012; Mittra *et al.*, 2014a, 2014b; Tait *et al.*, 2014).

We consider where guidelines or standards could contribute most effectively to the implementation of regulations in order to: support the speedy and effective delivery of innovation that safely meets public needs and desires; and where appropriate contribute more generally to the development of a thriving innovation environment in the UK (Synthetic Biology Leadership Council (SBLC), 2016).

1.4 Responsible research and innovation (RRI)

RRI is increasingly accepted by policy makers, government bodies and research funders (BBSRC, 2010; Technology Strategy Board (TSB), 2012) as an important component of governance systems in the EU, particularly for life science related innovation, but also in the context of other advanced innovative technologies. Seven major EU Framework Programme 7 research projects have been funded at a cost of 13M Euros and, although described as 'RRI', the focus has been mainly on research and not innovation (Zwart *et al.,* 2014). The emphasis is also mainly on stakeholder engagement as the key requirement to deliver 'responsibility' in research and innovation, but effective implementation of standards and regulations should also be a key requirement, as included, for example in the TSB (2012) Responsible Innovation Framework. Attention to RRI as an important component of governance is generally restricted to innovations that are seen as disruptive.

[4] https://www.gov.uk/government/organisations/accelerated-access-review

The sectoral focus of RRI, through these EU projects and other initiatives, is also shifting, from mainly GM-related aspects of life sciences to a much broader range of innovative technologies. However, there is little coordination across organisations tasked with implementing an RRI approach, and no consensus around what should constitute such an approach under the very different circumstances of (i) conducting basic research and (ii) the translation of that research to economically viable products and processes and (iii) the extent to which an innovation is disruptive or incremental. Looking at the manner in which RRI is currently being implemented in the EU, 'responsible behaviour' requires scientists and innovators to undertake effective public engagement about planned research and future innovative developments and then, supported by European policies, to adapt them where necessary to comply with the development of "… harmonious models for Responsible Research and Innovation that integrate public engagement, gender equality, science education, open access and ethics" (Geoghegan-Quinn, 2012). The absence of any reference to innovation or the societal benefits it may be able to deliver are notable, as is the assumption that there will be a societal consensus on which to base such policies at European level (Tait, 2009), and the lack of consideration of the potential of engagement initiatives to lead to greater polarisation of opinion rather than consensus (Sunstein, 2009).

1.5 Project objectives

The overall aim of the project is to develop a comprehensive framework to assess what mix of standards and regulations could be supported, and in what ways, in order to unlock the commercial potential of emerging technology value chains whilst ensuring safety and efficacy. The framework will be capable of adaptation to cover a range of technologies and applications in different sectors of the economy.

Based on the following objectives we have considered interactions between regulatory systems and guidelines and/or standards in general and in each of the three case study areas:

1. To understand which standards, policies or regulations/guidelines are most challenging to the achievement of future innovative potential.
2. To determine in what ways a more integrated approach, constructively linking guidelines and standards in support of a regulatory system, through government supported policy initiatives, could facilitate innovation without diminishing the safety and efficacy of products and processes.
3. To indicate what positive contributions could be made to these processes by having a standard for Responsible Research and Innovation.
4. To consider how such an initiative could best be aligned with the perspectives of key stakeholders in industry, regulatory bodies, public advocacy groups, trade associations.
5. Arising from these analyses, to develop a conceptual framework as a basis for sector-specific governance and regulatory decisions. When mature, this Governance Framework for Innovative Technologies will be demonstrated through a series of conceptual scenarios, modelling important systemic pressure points that could be moderated to inform the government regulatory approach that best supports both good governance and innovation.
6. Based on the conceptual framework, to apply our analysis: (i) to the case studies addressed in this project, and (ii) as a generic approach relevant to other advanced innovative technologies, including discussion of the approach and framework in a workshop with representatives of key stakeholders.

Objectives 1 – 3 above relate to development of the Framework itself and objectives 4 – 6 relate to use of the Framework to initiate change.

1.6 Structure of the report

Section 2 describes the research approach for this project, comprising: a literature review; a series of interviews with representatives of relevant constituencies, including companies, regulators, lawyers, policy makers and academics; and a stakeholder workshop to discuss the research outcomes and future research requirements.

Section 3 summarises the literature relevant to the development of an approach to proportionate governance of innovative technologies that integrates the roles of regulations, guidelines and standards.

Section 4 summarises the discussions with interviewees from the three case study areas to explore how our proposals could best be aligned with their perspectives, as a basis for further refinement of the proposed governance framework. A full report of the interview material is included in the Supplementary Report and a Summary Report is also available [http://www.innogen.ac.uk/reports/1174].

Section 5 presents our conclusions and the proposed Framework for Proportionate and Adaptive Governance of Innovative Technologies and describes how the framework could be used to address the issues addressed by this project.

2. Research approach and methods

2.1 Overall approach

Our approach to the research was based on the analytical framework developed by the Innogen Institute (Figure 1)[5]. The primary focus of the framework is on the **system** of interest for this project, the **value chain** for an innovation (the green arrow) requiring interaction of a sequence of company **business models** (blue arrows) working constructively together to deliver a product or process to a market. Where innovation is led by an MNC there may be one dominant business model, supported by several subservient models involving SMEs. Other value chains could include only a set of collaborating SMEs. For a disruptive innovation in the early stages of development, the challenge for developers will be to foresight the nature of potential future business models and the value chain to which they will contribute. For an incremental innovation, most of the value chain will already be in place and the task will be to fit a new business model into the overall value chain, or to adapt the existing value chain to a new element of the innovation environment (e.g. a new regulation or standard). The value chain is embedded within an **innovation environment or ecosystem** – including all the external factors that will affect the innovation process (the system of interest) and will determine, among other things, whether the innovative product or process is viable in the long run.

The key elements of interest for this project are the value chain itself, the regulatory system (including regulations, guidelines and standards), stakeholder engagement and RRI. A more integrated approach to dealing with these elements is proposed as the basis for a framework for analysis leading to a more proportionate and adaptive innovation environment, for both disruptive and incremental innovation.

2.2 Literature review

Our literature review primarily covered documents on standards and regulations and their impact on innovation, in general and in the case study areas. The outcomes of this review have contributed to our analysis in Sections 3 – 8. We have not had the capacity to do an extensive review of the current roles of standards and regulations/guidelines in contributing to either support for, or inhibition of, innovation in general or in the case study areas.

In addition to the fruits of our own literature search, several of our interviewees either directed us to, or sent copies of, reports and other documents relevant to the study.

2.3 Stakeholder interviews

Given the short timescale of the project, in recruiting participants for our survey we focused initially on Innogen Institute contacts, particularly those included in the Innogen Associates list (http://www.innogen.ac.uk/people/), and included others recommended by them. We interviewed twenty-five people, including representatives of large and small companies, not-for-profit organisations, and policy and regulatory bodies, along with academics and lawyers (see Annex 1).

Each invited interviewee was sent an outline of the project (Annex 2) and an interview schedule (Annex 3). Given the range of interests and expertise among our interviewees, the interview schedule was used as a guide for a structured conversation about the issues raised to stimulate the emergence of new ideas or novel juxtapositions across the various elements of our analysis. This approach encouraged interviewees to contribute ideas based on their experience in areas not

[5] http://www.innogen.ac.uk/downloads/Innogen-Institute-Research-Outline.pdf

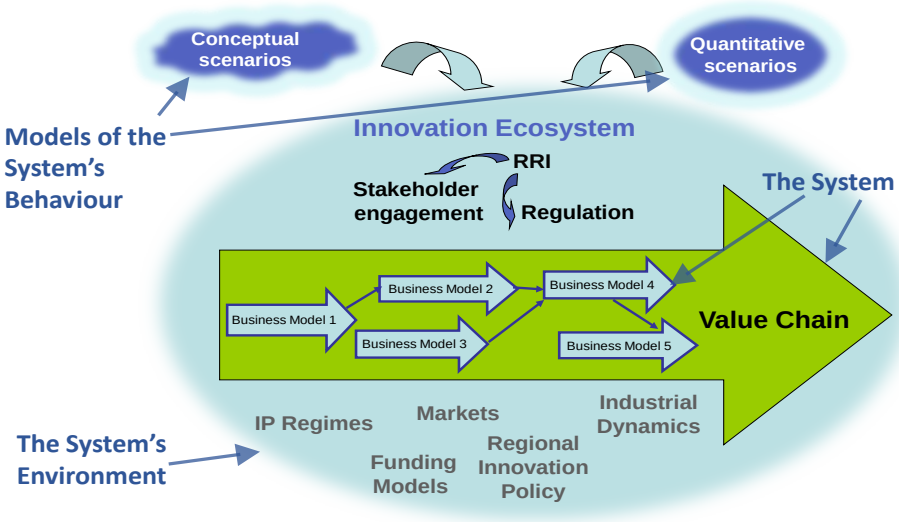
covered by our case studies and, given the exploratory nature of the project, we welcomed these inputs.

General and cross-cutting comments are reported in Section 4.1. Regulation of pharmaceuticals, bio-pharmaceuticals and other health-related technologies is very relevant to the current governance of personalised medicine manufacture and autologous cell therapies, and these issues are included together in Section 4.2. Likewise, regulation of genetically modified organisms (GMOs) is the template on which regulation of synthetic biology and industrial biotechnology is being modelled and so these issues are included in Section 4.3. Regulation of information technology systems and also of finance systems is relevant to the FinTech case study and so these issues are included in Section 4.4.

The interviews were conducted by telephone and were recorded and transcribed for analysis. A summary of the outcomes of this analysis are included in Section 4, and a full description can be found in the Supplementary Report [http://www.innogen.ac.uk/reports/1174].

The experiences and perspectives of interviewees varied depending on their professional expertise and the sectors they have worked in (see Sections 4.5 and 4.6). Understanding the background to the divergent views expressed by our interviewees about the nature and extent of problems in specific areas and also how divergences might be resolved, is an important aspect of judging how the overall governance process in different areas can usefully be adapted and the role of standards in contributing to that adaptation.

Figure 1. Innogen Institute Research Framework



2.4 Stakeholder workshop

A workshop was held to explore the views of a range of stakeholders on the issues raised in this report and the proposed Governance Framework for Innovative Technologies, focusing particularly on the following questions:

1. Where are there roles for standards in contributing to the proportionate governance of innovative technologies?

2. Where and how could the proposed framework facilitate safe, effective and economically viable innovation, both disruptive and incremental?
3. Are there opportunities, based on a more integrated involvement of standards, guidelines and regulations, to increase the confidence of stakeholders (particularly citizens and advocacy groups) that an industry sector is being well managed and governed, e.g. through an extended RRI approach.

The Governance Framework is designed to be adaptive to cover a range of technologies and applications in different sectors of the economy. It could enable regulators, policy makers and standards bodies to assess what mix of standards and regulations could be supported, and in what ways, in order to unlock the commercial potential of existing and emerging technology value chains whilst ensuring quality, safety and efficacy. The outcomes of the Workshop are reported in Section 4.7.

3. A proportionate and adaptive governance system for innovative technologies

3.1 Delineating the roles of regulations, guidelines and standards

There is a lack of consistency in the use of the terms 'regulation', 'guideline' and 'standard'. Even within the restricted context of the governance of innovative technologies, there is variation across countries, across sectors and at different stages of the innovation process. This project focuses on the relatively orderly, authoritative and widely applicable types of standard developed by national standards bodies (NSBs) and international standards organisations, and compared the roles and impacts of such standards to those of regulations and the guidelines developed by regulators in support of regulation (BSI, undated-b). We have *not* considered the wider world of standards development, described by Busch (2011) as a 'cacophony of governance', where groups of companies, lobby groups, etc. develop their own independent standards for a variety of purposes, including protection of intellectual property and creation of competitive advantage, implemented through market-related mechanisms or through the authority of trade associations. The use of the word 'guideline' is equally difficult to pin down, given that any organisation can set up guidelines to meet a variety of needs.

For this report, we have used the terms as follows (see Table 1):

> *Regulation:* legally based instruments, backed up and enforced by a government authority, a mainly unambiguous category;
>
> *Guideline:* issued under the aegis of a regulatory system to help those being regulated to understand what is expected of them by the regulator;
>
> *Standard:* an agreed way of doing something (making a product, managing a process, delivering a service or supplying materials); the distilled wisdom of people with expertise in their subject matter, who know the needs of the organizations they represent (manufacturers, sellers, buyers, customers, trade associations, users or regulators)[6]
>
> *Consensus (in relation to standards)* (BSI, 2011): having general agreement, characterized by the absence of sustained opposition to substantial issues by any important part of the concerned interests and by a process that involves seeking to take into account the views of all parties concerned and to reconcile any conflicting arguments. Consensus need not imply unanimity.

The guidelines discussed in this report are generally devised as components of a regulatory system, with standards being treated as part of a separate system because of their very different development process and mechanism of implementation (see Figure 2). However, these distinctions do not always hold up in practice. Guidelines may have much in common with standards and in some contexts either could be used with equal effect, playing a subservient role to regulations in the governance of a particular sector. Both guidelines and standards can acquire legislative authority where they are seen as meeting the requirements of a particular regulation, if so designated by the regulator. In such a case the standard becomes equivalent to a guideline according to the above descriptions.

Table 1 summarises some of the presumed distinguishing features of standards and regulations/guidelines, illustrating the point that standards, developed by a consensus process

[6] http://www.bsigroup.com/en-GB/standards/Information-about-standards/what-is-a-standard/

involving a broad range of stakeholders have the potential to be more flexible and adaptive than guidelines developed by regulatory bodies, although this does not hold under all circumstances[7].

Table 1. Differences between standards and regulations/guidelines, and relative advantages

Standards	**Regulations/Guidelines**
Based on recommendations	Based on legislation
Adoption is usually voluntary	Adoption is mandatory for regulations and potentially so for guidelines (soft law)
Established by consensus of all parties concerned, including relevant industry sectors	Developed by a regulatory authority, usually involving consultation
Based on consolidated results of science, technology and experience	Guidelines provide technical specifications either directly or by reference, e.g. to standards
Approved and published by recognised standardisation body	Adopted by a legal authority
Oversight by independent third party certification	Oversight by formal government-appointed regulatory bodies
Advantages of standards	**Advantages of regulations/guidelines**
Standards can act as infrastructures for coordination; a common language for interoperability and compatibility.	Regulations have the force of law and compliance is compulsory and enforceable.
Standards as routines (usually internal standards) can govern behaviour required for certain activities/routines.	Easier to diffuse through inter-country, regional or international treaties and conventions.
Standards as technology can reduce variety and enhance economies of scale thereby reducing transaction costs.	Regulations are prescriptive, and sometimes are linked to specific guidelines and/or standards which if adhered to constitute compliance
Standards can be an innovation to achieve market dominance.	

Source: adapted from Allen and Sriram, (2000), Langlois and Savage (2001)

3.2 BSI role in standards development

Since its inception in 1901 the BSI has led nationally and internationally on the development of voluntary consensus standards, beginning with technical product (interoperability) standards and then moving into process standards, assuring the quality of manufacturing processes (e.g. the environmental management standard (BS ISO 14001)). A more recent development is the creation

[7] For example, the monographs, standards and guidances developed by the European Pharmacopoeia are in practice closer to regulatory guidelines than to standards, often being invoked formally by regulators to specify compliance with a regulation.

of standards covering the principles required for good business practice, such as *Guidance on Social Responsibility* (BS ISO 26000), sometimes described as 'aspirational standards'. This could be a potential starting point for a standard on RRI.

The International Organisation for Standardisation (ISO) brings together 162 national standards bodies "… to share knowledge and develop voluntary, consensus-based, market relevant International Standards that support innovation and provide solutions to global challenges"[8] . A range of other bodies are also involved in international governance of technologies, including the World Trade Organisation (WTO), World Health Organisation (WHO), World Intellectual Property Organisation (WIPO) and, in health-related areas, the system of national and international pharmacopoeias that furnish quality specifications for active pharmaceutical ingredients (WHO, 2013).

BSI full consensus documents (British Standards) are prepared by a committee and involve broad consultation as part of the approval system. They take some time to produce and for the agreement to go through public review - twelve to fifteen months for a national standard and up to 3 years for an international one. [Some regulations take considerably longer to develop but on the other hand, given a strong political mandate, regulations can be produced or changed relatively rapidly].

The following types of full consensus standards are listed by BSI (2009):

- Specification – outlining performance and/or design and/or service requirements that need wide consensus;
- Method – focusing on the way products and materials are tested or the way they are specified;
- Vocabulary – defining terms used in a sector or technology;
- Code of Practice (CoP) – Guidance and recommended options from outline design to workmanship and safe practice;
- Guide – general guidance with recommendations and background information, less specific and more discursive than a code of practice.

BSI also develops related publications or partial consensus documents that are useful for fast-changing technology sectors where it may be important to agree on a technical solution and publish it quickly before going through the checks and balances needed for a full British Standard. The following such documents may be relevant to this project:

- Publicly Available Specification (PAS) – a sponsored standard developed quickly (within 12 months) without requiring full consensus; it can be detailed and solution-specific (BSI, 2009).
- Framework Standard – voluntary consensus standards, providing a stimulus for innovation through shaping best practice (Steedman, 2013).

3.3 Standards, innovation and economic benefits

This report considers the potential relative and complementary roles of standards and regulations/guidelines in unlocking successful innovation and accelerating commercialisation of new technologies, at the same time ensuring quality, safety and efficacy in products and processes (see Figure 2).

[8] http://www.iso.org/iso/home/about.htm

Discussing the role of standards in contributing to innovation, BSI has highlighted a range of attributes that could potentially enable standards to facilitate innovation processes in life science-related areas and in new areas where advanced innovative technologies are beginning to be subject to a governance process (BSI, undated-a). Key aspects are the consultative nature of the process of standard development, involving a broad range of stakeholders, and the availability of fast-track mechanisms such as the PAS that can set out common metrics, terminologies or concepts to enable businesses to innovate in advance of the development of a full consensus standard.

The following aspects of standards (see Table 1) are particularly relevant to this project:

- The collaborative nature of the standards development approach frees innovators to concentrate on finding ways to differentiate their products and services, especially in areas of mutual benefit where they can reduce variety and transactional costs.
- In the establishment of a market, standards allow investors to understand what the investment will involve and enable companies and developers to describe their products and services in marketable terms.
- Standards provide independent assurance and accreditation of, for example, safety, quality and efficacy of products and processes and this can be critical in gaining public acceptance of new technologies.
- Standards can contribute to procurement decisions by clarifying how innovative products and processes can be measured against each other and against existing products.
- By evolving as technology develops, standards can be used to set targets for technologies to aim for in future, in terms of performance indicators.

Through their impact on R&D, production, manufacturing and market penetration standards can clearly contribute to the economic success of sectors and nations, and can promote innovation and shape markets (Tassey, 2000). Depending on the type of standard, the economic impact can be at the micro- or macro-economic level. At firm, industry or market levels standards can reduce transaction costs and improve competition and technology selection; at the macro-economic level effective standards can have an impact on growth of national economies (Blind et al, 2010). A useful analysis of the economic impact of standards by Blind and colleagues (Blind et al., 2011; Blind, 2013) (Table 2) shows the contribution of information codified in standards and technical rules to the growth in GDP in a range of countries with the conclusion that standards have a positive influence on economic growth based on better diffusion of knowledge.

Table 2: Effect of standards on economic growth in five countries

Country	Period	Growth Rate of GDP	Contribution of Standards
Germany	1960-1990	3.3%	0.9%
	1992-2006	1.1%	0.8%
France	1950-2007	3.4%	0.8%
United Kingdom	1948-2002	2.5%	0.3%
Canada	1981-2004	2.7%	0.2%
Australia	1962-2003	3.6%	0.8%

Source: Blind *et al* (2011) and Blind (2013)

Standards and standardisation can also have an impact on economies through the operation of health, safety and environmental standards in reducing occupational accidents and protecting the environment, leading to better quality of life and sustainable practices (Blind, et al, 2011).

The logic in these analyses uses the stock of standards in a nation as a proxy for codified knowledge which can be easily and affordably diffused, based on consensus standards. Blind's analyses do not include proprietary (sponsored) standards or those developed by national industry consortia with the strategic intention of market capture and dominance, especially in technology sectors such as ICT (information communication technologies) where the choice of platform technology standards can determine the relative competitive advantage of a technology and its trajectory.

Given the broad range of benefits conferred by standards it is clear that they could have a substantial economic impact on the nations and industry sectors to which they contribute[9]. A recent report on the economic contribution of standards to the UK economy (Centre for Economics and Business Research Ltd. (CEBR), 2015) described the important role that standards can play in supporting economic growth through boosting productivity and innovation, opening up new markets and linking UK companies into global supply chains and reducing technical barriers to trade. However, it is also clear from the interviews in this report that inappropriate, poorly specified or insufficiently adaptive standards can have seriously negative impacts on innovation and the economic competitiveness of companies and countries and this factor is generally not covered in published economic analyses.

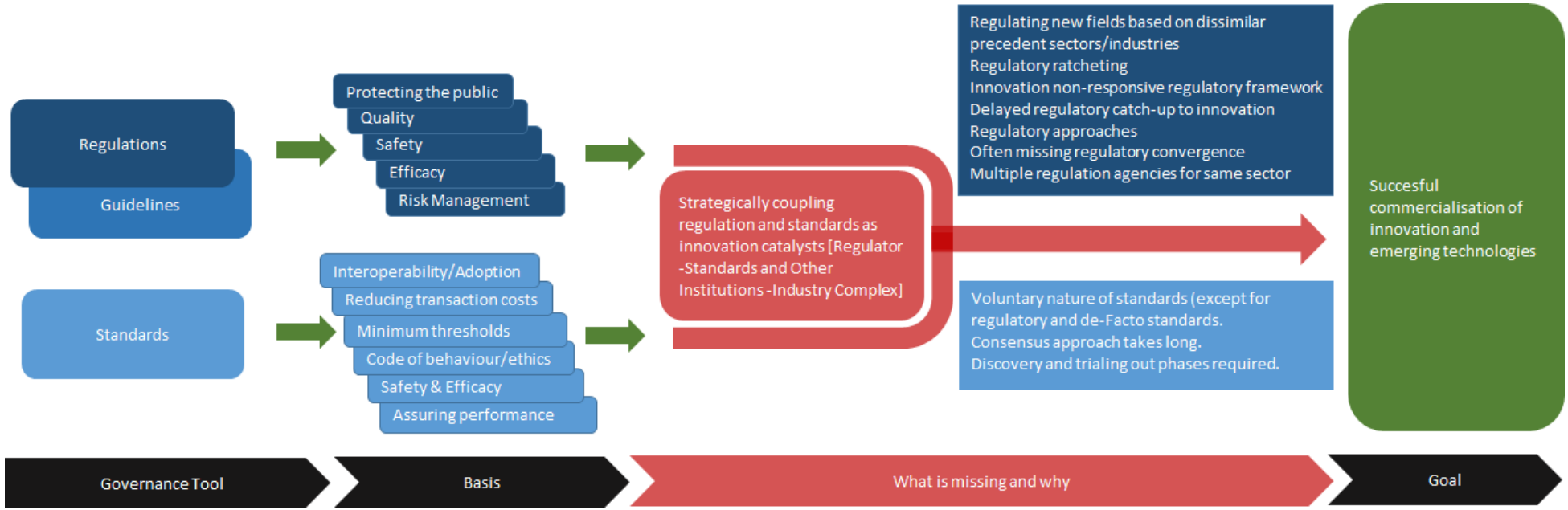
Given the very different roles of standards in different industry sectors, it is not appropriate to attempt to aggregate economic benefits of standards across sectors or across different stages in the development of an innovative technology. In the context of product and process standards (Table 3), it should be possible, on a sector-by-sector basis, to provide a reasonable estimate of the economic value of standards, but this would need to take account of the extent to which the relevant standards were fit for purpose and were indeed supporting, and not inhibiting, innovation. We are not aware of any such analysis.

Conducting an economic analysis to quantify the benefits of a PAS or Framework standard is considerably more complex and subject to high levels of uncertainty, and it would be even more challenging to calculate the economic value of a standard to be used in the early development stages of a disruptively innovative technology, as a prelude to the drafting of a guideline or a legally based regulation.

This report describes a new approach to integrating the roles of standards, guidelines and regulations to support innovation. It is legitimate to claim that considerable economic value could arise from such an initiative and, once implemented, a targeted data collection initiative could enable the economic value of these standards and regulations to be more reliably assessed.

[9] http://www.iso.org/iso/home/standards/benefitsofstandards/benefits_repository.htm?type=EBS-MS

Figure 2: An analysis of the complementary relationship between standards, regulations and guidelines to stimulate innovation



3.3.1 Role of standards in reducing the variety of goods and services

One claimed advantage of standards is their role in reducing the variety of goods and services to an optimal level for minimising cost (Blind, 2009). This can indeed be an advantage for incremental innovation where it is relatively straightforward to compare a range of possible product or process-related options for improving the operation of an existing value chain. However the situation is different when dealing with radical innovation at the early stages of development, for example cell therapies and regenerative medicine. In such cases it is often unclear what will be the 'winning' approach to the development of the new scientific discoveries, but at the same time there is strong pressure to develop standards, regulations and guidelines to ensure the safety, quality and efficacy in use, and also to enable potential investors to judge the value of a potential investment. Premature adoption of a regulatory system that then takes a dominant role in shaping the innovation environment for the potentially disruptive technology, and is subsequently difficult or impossible to adapt, can severely constrain the nature and quantity of the eventual societal benefits[10]. These pressures run counter to the need to support a variety of innovative options in the early development phase to allow the optimal form of a disruptive innovation to emerge and then to be governed by the most appropriate combination of regulations and standards.

In the early stages of development of disruptive innovation, there is a period during which such pressures should be constrained to some extent. The technological variety that exists in the early stages of development of a disruptive set of innovations should ideally be allowed to evolve in response to the full range of ecosystem influences (Figure 1). This would mean postponing the choice on development of a regulatory system until there is some clarity about the potential evolutionary pathway of a radical innovation, and then choosing a regulatory system that fits with the expertise of the most appropriate industry sector to take up development of that technology (Tait and Chataway, 2007; Chataway *et al.,* 2006). Some time will be needed, perhaps running into a number of years, to allow sufficient knowledge to emerge to enable rational decisions to be taken on such questions.

3.3.2 Types of standards and their impact on innovation

Blind (2009) characterised standards into four categories: compatibility/interoperability, minimum quality/safety, variety reduction, and information: we have added one further category, Framework Standard (Steedman, 2013), to include the type of aspirational or behavioural standard that we believe will be particularly important in the context of this report (see Table 3).

[10] An example from the past is the adoption of pesticide-related regulatory approaches for GM crops, rather than treating them as novel plant varieties. If treated as new plant varieties they would have been developed by seed companies rather than the agrochemical industry, there would have been a different set of first generation crops and the European societal concerns about this technology may not have emerged (Tait, 2007; 2008).

Table 3: Types of standard and their effect on innovation

Type of Standard	Positive Effects	Negative Effects
Comparability/Interoperability ▪ Process standards ▪ Product standards	• Network externalities • Avoiding lock-in old technologies • Increasing variety of system products • Efficiency in supply chains	• Monopoly power • Lock-in old technologies in case of strong network externalities • Path dependence if chosen standard came from a non-optimal selection process (see variety reduction)
Minimum Quality/Safety ▪ Product standards ▪ Process standards ▪ Organisational behavioural standards	• Avoiding adverse selection • Creating trust • Reducing transaction costs	• Raising rival's costs • Competitive barrier to entry for new resource-poor entrants by 'gold plating' of standards by incumbents
Variety Reduction ▪ Process standards ▪ Product standards	• Economies of scale • Critical mass in emerging technologies and industries	• Reducing choice • Market concentration • Premature selection of technologies • Stifling alternative development (innovation) pathways
Information ▪ Product standards ▪ Process standards	• Providing codified knowledge	• Barrier if codified knowledge is proprietary or expensive to incorporate
Framework ▪ Aspirational/behavioural standard	• Delivering equitable relationships across companies and sectors • Contributing to 'responsible' company behaviour	• Can be seen as a barrier to trade

Source: adapted from Blind (2009); Steedman, 2013.

4. Stakeholder perspectives

This section describes key insights from the interviews we conducted with stakeholders, full details of which are included in the Supplementary Report [http://www.innogen.ac.uk/reports/1174]. Section 4.1 covers the general points raised by interviewees. Sections 4.2, 4.3 and 4.4 relate specifically to the three case studies (personalised medicine manufacture for autologous cell therapies, industrial biotechnology/synthetic biology, and financial technology (FinTech) respectively). Section 4.5 summarises the differences across sectors; and Section 4.6 summarises the different perspectives of stakeholders with different areas of expertise. Section 4.7 summarises the main points raised in the stakeholder workshop.

The interviewees were all experienced in their fields and we took the opportunity to ask them about the governance background for the technologies with which they engage, to contribute to exploration of future roles for standards in supporting a broader range of innovative technologies. The small number of interviews overall means that we cannot draw firm conclusions for any of the sectors studied. However, the project does form a useful basis for future investigations and decision making in this area and for proposing a supportive framework for such decisions.

4.1 General issues raised by interviewees

4.1.1 Lack of coherence in the current system

This project was faced with a complex set of interactions arising from the development and adoption of guidelines and standards across numerous industry sectors by equally numerous bodies exercising some form of governance role, the variable nature of the instruments described as standards or guidelines, and their diverse relationships to legally binding regulations (Busch, 2010). The issues raised in this project were described by interviewees as having been in people's minds for some time, but not often talked about.

Our approach, as summarised in Section 2.1 and Figure 1, was regarded by our interviewees as a sensible basis on which to build. However, it was clear that some entities labelled as 'standards' did actually have the authority of regulatory guidelines; likewise some interviewees referred to 'guidelines' as being merely advisory with no real enforcement process behind them. So, although our general categories were seen as a valid simplification, this research (and any future research) will need to be alert to these semantic variations. The key distinction to make is between governance instruments that are subsidiary to legally-based regulatory systems (described as guidelines in this report) and those such as consensus standards that operate in parallel with regulatory systems and are overseen by independent third party certification. Interviewees emphasised that issues of safety, quality and efficacy will demand the rigorously enforced compliance achieved through a legally based regulatory system, but they also recognised that there may be mechanisms by which this compliance can be delivered in 'smarter' ways than is currently envisaged in some regulatory systems and still be proportionate.

In the governance of health-related innovations, the 'reference standards' of the European Pharmacopoeia were seen as the most important legally binding guidelines in meeting the regulatory requirements for bio-pharmaceutical and biosimilar drugs manufactured using synthetic biology-related processes, or for cell therapies. Some interviewees saw the Pharmacopoeia process as opaque and rooted in historically imposed rigidities, observing that, while it is effective in devising standards for relatively simple, routine extensions to existing products and processes it may not be able to adapt effectively to the needs of innovative new technologies, particularly those arising from advanced biotechnologies.

In other areas interviewees had seen flexibility in the application of a regulatory guideline so that, where an innovator had adopted a different route to compliance, regulators were open to explanations of how the alternative resulted in an equivalent outcome. However the availability of this usefully flexible and adaptive approach was seen as being dependent on the idiosyncrasies of individual regulators, rather than the nature of the guidelines themselves.

4.1.2 Towards adaptation and integration

The ideal principle for the governance of innovative technologies was seen to be to couch legally binding regulations in very general terms related to the desired outcome of the regulation and include detailed procedures and expectations in the guidelines and standards that are subsequently drafted in collaboration with a broad range of stakeholders, with varying degrees of democratic participation, depending on the context and the expertise required.

However, experience of past governance challenges, of current adaptation or non-adaptation of regulatory systems, and of expected future challenges from innovative technologies, varied from one industry sector to another and from one country or region to another. Therefore any framework proposed to support future adaptation towards greater proportionality in the governance of innovative technologies will itself need to be flexible and adaptive to a variety of needs and contexts.

It clearly was not possible to generalise across sectors and regulatory systems about the relative ease and rapidity of setting up new regulations, guidelines and standards, or about the ease of adaptation of existing instruments. The need for consensus in standard building can extend the development or adaptation timescales. The involvement of governments in the development of regulations can very effectively speed up the introduction of a regulatory system if deemed necessary, but interviewees recognised that the resulting regulatory systems can in some cases prove to be misguided and can then prove very difficult to adapt to the needs of emerging technologies. The life science industry sectors were described as seeking a new basis for governance, a new consensus, but struggling to work out what the new operational model would look like.

4.1.3 'Gold plating' vs proportionality

Some interviewees referred to the 'gold plating' of UK regulations in going beyond the minimum requirements of an EU Directive in translating it into UK law (see also Table 2). There is a perception among some UK policy makers that such gold plating will lead innovative companies to locate in the UK in order to benefit from the kudos of meeting such demanding regulatory requirements. However, there is no evidence for this effect; indeed there is strong evidence to the contrary, justifying government initiatives to remove such regulatory over-enthusiasm.

The issue of 'gold plating' has some counter-intuitive aspects. It can, for example, be welcomed by large companies with the capacity to meet such standards, as a 'barrier to entry' to discourage competitors from entering a particular field of development. Even small companies who have already begun to negotiate a difficult regulatory system may oppose subsequent moves in the direction of greater proportionality for that system, given that it would increase the level of competition. There may thus be opposition to adaptation in the direction of greater proportionality from incumbent companies already operating in a particular area, who would see it as a device to open up competition to a broader range of companies. Where the innovation concerned is disruptive, this effect can be particularly powerful. Indeed it can be claimed to have shaped the current structure of the pharmaceutical and agro-biotechnology sectors (Tait *et al.,* 2007; Tait, 2007).

Consultants and advisors may also be reluctant to embrace any moves away from gold plating that would diminish demands for their expertise. One of our interviewees also noted that institutional inertia may mean that, even following removal of requirements related to gold plating, actual practices on the ground have not been changed.

These factors are contrary to more general government moves in the direction of proportionality and will in the long run increase industry costs and reduce the amount of innovation that is successfully developed. Also, one interviewee described how the process of exceeding the regulatory requirements in one area could undermine the value of regulations and standards where they are justified in another area.

Not un-related to 'gold-plating', regulators in some areas were seen to be indulging in 'mission creep' (a gradual but significant enhancement of the regulatory system with no corresponding reduction in unnecessary regulatory requirements, also sometimes described as 'the regulatory ratchet'). There clearly is a need to continue to ensure safety etc. but this is an area where the governance process in general could usefully devise an approach to dealing with disruptive innovations that enables further development without requiring legislative change and without leading to legal challenges.

4.1.4 Maintaining or reducing variety – a timing issue

One of the advantages ascribed to standards is their ability in some cases to reduce variety, providing economies of scale and supporting the acquisition of critical mass in emerging technologies or industries (see Table 2). However, with a disruptive innovation in its early stages of development when it is still unclear what can be delivered, far less what risks and benefits will be entailed, premature reduction of variety can close off important future avenues to meeting societal needs (see Section 3.3.1 and Table 3).

So the process of reducing variety has both benefits and disadvantages and, particularly for a disruptive innovation, these will be unevenly distributed across different scales of company within a sector and across industry sectors. For a large company with sufficient resources to take an innovative product all the way to a market, the extent of disruption of current value chains is likely to be an important consideration, potentially excluding some of the most innovative applications. For a small company, there will be a tension between a desire to optimise the opportunities arising from an innovation and the need for investment (most likely from venture capital) where the investor will want to know what regulatory system will be in operation for the innovation in order to judge the value of the investment.

To date such decisions have been determined by serendipitous interactions among companies, trade associations, policy makers and regulators and the scale of the challenge to human foresighting capacities probably rules out any other approach. However, maintaining variety for as long as possible, in the face of the competing pressures, may be a useful rule of thumb and, as we propose here, standard setting may have a useful role to play in this process.

4.1.5 Degrees of transparency and of consultation with stakeholders

There were differences of perspective among interviewees on the degree of transparency around the development of standards, guidelines and regulations. Those closest to the development of regulatory systems felt that their public consultation approach led to more openness than in the development of standards. However, those more closely involved in the development of standards felt that the process was more open and consultative. This difference needs further exploration but seems to be related to requirements for a broad range of expertise to be involved in the development of a consensus standard, and the fact that such a standard cannot be achieved

without consensus; whereas although regulations are more open to public commentary the regulator has the final say in the outcome. This means that regulators can drive through a regulatory guidance in a relatively short period if they compress the time available for consultation and have only one round of consultation, but this can then lead to unresolved conflicts.

The generalisations that (i) regulations are developed on a less consultative basis than standards, (ii) standards can be developed more rapidly than regulations, and (iii) regulations and guidelines are harder to adapt than standards, were not borne out in interviews. Counter examples were produced to all these assumptions, but it was apparent that the leading role of companies in developing standards was important for understanding of the technological opportunities created by an innovation and of the impact of specific regulations or standards on these opportunities.

Several interviewees remarked on the lesser value of standards in a governance system because the standards bodies did not have in-house expertise in specific technology areas. However, this demonstrates a misunderstanding of the role of standards bodies which is to convene the appropriate array of expertise within the stakeholder teams they set up to develop a standard, usually in response to an initiative proposed by a group of stakeholders. The in-house expertise in a standards body is in the process of achieving a standard, which varies across the broad range of possible types of standard, including the necessary skills in consensus building.

4.2 Personalised medicine and cell therapy/regenerative medicine

4.2.1 Future products and their governance

Cell therapies/regenerative medicine is a complex field building on the use of engineered cells, tissues, biomaterial scaffolds, growth factors, or combinations of them to help the human body augment, repair, replace or regenerate organs or tissue that have been damaged by disease (Wang, 2013). These therapies can be autologous or allogeneic[11] and the main focus of our interviews was on autologous therapies as an example of personalised medicine, in that patients are treated with a modified version of their own cells[12]. The players in cell therapy manufacture include large commercial organisations, SMEs, not-for-profit organisations such as Scottish National Blood Transfusion Services (SNBTS), and academic institutions. This diversity of players brings challenges in regulating the sector and the need to identify adaptive and proportionate regulation. Discussions in this case study often strayed into pharmaceutical regulatory systems given that this was chosen as the appropriate regulatory precedent for these innovations.

For regulatory purposes, autologous cell therapies are classed as Advanced Therapy Medicinal Products (ATMPs), regulated at the EU level under the Tissues and Cells Directive 2004/23/EC and the ATMP Regulation 1394/2007[13]. The two key requirements of the regulatory system are that: all ATMPs must go through ***clinical trials*** in the same way as other medicines; and all ATMPs to be placed on the market in the EU must have a ***marketing authorisation.*** The decision that ATMPs must go through clinical trials in the same way as all other medicines has required lengthy discussion (still on-going) between innovators and regulators on how to adapt the chosen

[11] ***Autologous cellular products*** – patients are treated with a modified version of their own cells.
Allogeneic cellular products – patients are treated with cells from a single donor multiplied on a large scale and distributed widely.

[12] For example in cancer treatment, personalised medicine classifies tumours according to their genetic make-up instead of where they grow in the body, such as 'prostate' or 'breast' cancer. People with the 'same' cancer can have different forms of the disease so responses to treatment can vary and cancers growing in different parts of the body may also share the same genetic faults so respond to similar treatments.

[13] https://www.gov.uk/guidance/advanced-therapy-medicinal-products-regulation-and-licensing

chemicals-based regulatory system to the needs of biological products and processes (Mittra *et al.,* 2014b).

The inherent variability of living therapies makes standardisation of manufacturing a complex process. Innovate UK and BSI have suggested that Design for Manufacture (DFM) standards could be a useful framework for standards that can catalyse innovation in cell therapy manufacture (Sheridan and Ginty, nd) with the intentions: (i) to improve regulatory success rate by helping the design of high quality repeatable manufacturing processes; (ii) to accelerate the launch of new products on the market; and (iii) to reduce investment costs necessary to launch a product onto the market. The following standards have so far been developed for regenerative medicine:

1. PAS 83:2012 Developing human cells for clinical applications in the European Union and the United States of America. Guide
2. PAS 84: 2012 Cell therapy and regenerative medicine. Glossary
3. PAS 93:2011 Characterisation of human cells for clinical application. Guide.
4. PAS 157:2015 Evaluation of materials of biological origin used in the production of cell-based medicinal products. Guide

4.2.2 Interviewees' perceptions of governance issues

This area is characterised by a lack of full scientific understanding of the mechanisms of action for cell therapies, leading to variability in the quality of the science underlying the development of novel therapies, and lack of good understanding of the science and its limitations by regulators. Another perspective on the challenge of governing this field referred to the difficulty of juxtaposing biology, medicine and manufacturing and allowing iteration among these elements. The field is dealing with disruptive innovation, at the cutting edge of science, with no road-map, and no clear information on future regulatory requirements. However, given that the products are to be administered to patients there is an absolute requirement to ensure that therapies will not cause harm, key principles in the formulation of a product being:

(i) the patient should receive no substances that they do not need to receive, and
(ii) they should not receive any more of any substance than is required for its purpose.

This area was seen to be one where the process of choosing the regulatory precedent for a new application is opaque to innovators who are not aware of the preceding standard being used by the regulator. An appropriate precedent for regulation of cell therapies was seen to be the system used for blood products where standards have now converged over a period of around 70 years on an international norm. Some cell therapeutic spaces were described as the 'Wild West', where attempts to introduce standards have not had the granularity to deal with different kinds of stem cells and there are large numbers of clinical trials across the world based on cells that have not been fully characterised.

From the industry perspective there was reference to manufacturing standards being used as competitive tools – companies use standards to set the bar high and manufacture to that high threshold to outcompete others. In the context of choice of regulatory precedent, industry interviewees also saw cracks appearing in the current regulatory system in that the regulation of devices, synthetic pharmaceuticals, biotechnology products and ATMPs all exhibit path dependencies – each stage of regulation was built on the shoulders of preceding (chemical) regulation, and cell therapies (ATMPs broadly) have different therapeutic features from these preceding therapies. For example, one can analyse chemical entities for impurities but this is difficult for ATMPs.

In medical related areas most interviewees commented on the open-ness of regulatory authorities, including the FDA and the EMA, and their willingness to come to an understanding on the science without unnecessary bureaucracy. However, there were also comments on the relative competitive positions of different types of players in the pharmaceutical sector and the need to focus in future on targeted, rather than blockbuster, markets. In this context, the roles of standards, regulatory guidelines and regulations and how they interact with one another, are not well specified and standards play an important role (number one in the hierarchy) for the initial development of new technologies, followed by guidelines and then regulations.

4.2.3 Relative roles and interactions of regulations, guidelines and standards

Generally speaking the role of standards was much less prominent for those interviewees dealing with regulation in the context of clinical trials than for those involved in cell manufacture where they are expected to understand the available standards that could be helpful to them. When it comes to getting a product into the clinic or onto a market the regulatory authorities and their guidelines are more central. However, there were several references to regulatory systems that are based on assumptions dating from previous chemical areas of application being difficult to adapt to the needs of a new generation of biological products.

There was considerable discussion in this case study of the role of the system of pharmacopoeias. The European Pharmacopoeia has been involved in developing standards in advance of setting up more rigid requirements linked to EMA regulations, with stakeholders playing a prominent role. There is flexibility in this case – where a product developer wants to do something differently from the guidelines or pharmacopoeia standards in operation, they can inform the EMA who may agree that the proposed change is equivalent to the standard or guideline. There were several examples where ISO standards had been adopted by pharmacopoeias, giving them a status similar to those of regulatory guidelines.

One criticism of the European Pharmacopoeia, given its essential role in meeting the regulatory requirements of the EMA, was the high cost of gaining access to the standard. It was also noted that the pharmacopoeias in general seem to be hard-wired into the psyches of different global regions and may be an important part of the rigidity and inflexibility of regulatory systems. An example of the role of vested interests in standards development was also described where the International Pharmacopoeia, attempting to apply an even-handed process to developing an international monograph setting a standard for antibodies, found that some innovating companies attempted to block this process and to set the bar impossibly high for follow-on companies. Another problematic issue mentioned was the BSI involvement in the development of a raw materials standard at the same time as a parallel initiative under the European Pharmacopoeia, duplicating effort and increasing complexity.

4.2.4 Flexibility and adaptiveness of governance systems

Unlike other life science areas, there was a high level of agreement in this case study that EU regulators were very open to discuss regulatory questions with companies and others, specifically generic principles about how to solve problems, so long as they are not seen to be advising industry. There is an onus on regulators to update guidelines based on experience from reviewing dossiers and finding new elements. Equally there is an onus on industry to make sure that the information they provide to regulators is up-to-date and these factors contribute to making European regulatory guidelines more solid documents. There is also a new spirit of willingness in the last year for regulators to contribute to innovation agendas and standards, as part of this process, and this could be a good catalyst for getting innovations to the clinic, but it is important that corporate or national interests do not drive the development of a standard.

4.2.5 Issues related to disruptive and incremental innovation

Some interesting points emerged from this case study in the context of choice of appropriate regulatory precedent for a disruptively innovative technology. In developing the ATMP regulation for cell therapies, because of the need to involve all interested parties, workshops were organised to include the medical device industry, those developing medicinal products and patient representatives. The medical device aspects of the innovative technology were considered easier to control than the biological aspects, given the latter's risks of viral contamination and related public health issues. The view that the greater public health issues were on the biological side pushed the regulation in the direction of the precedent of the existing drugs regulatory system.

An alternative example was the regulation of the first recombinant DNA product to be proposed for a clinical trial in the UK in the 1980s. Discussions between the industry and regulators led to an approach that did not follow a chemical precedent, the first UK guideline on manufacture and control of a rDNA product, subsequently shared with twelve other EU states. The interviewee who quoted this example was of the opinion that it should never happen that new biological products are forced into regulation through a chemical-based system.

Interviewees pointed out that the process of adapting chemicals based regulatory systems to govern innovative biologically based products is not new and, at least for incrementally innovative products, the regulators have learned from experience in development of biosimilar monoclonal antibodies. These products were relatively well characterised but could not be treated as straightforward chemical entities and regulators used the concept of comparability, setting a pattern for other types of biological product. Today, this approach is much better informed and more pragmatic than it was ten years ago and factors influencing this greater flexibility have been the number of fora where industry can talk to regulators and the rise in collaborative efforts involving companies, universities and not-for-profit organisations.

In the development of biosimilar products (incremental innovation) some companies in the USA had a corporate policy not to cooperate in the process so as to make it more difficult for new companies to enter this area. However, other companies did collaborate and indeed supported the development of standards for biosimilars, supported by European bodies that were looking to encourage small companies.

The idea that, for more disruptive innovation, one would focus on standards, rather than a regulatory approach in the early stages, was seen as appropriate by some, although it would be made more difficult by the need for innovating companies to talk to one another, given the competitive nature of the industry. However, this progression from standard to guideline to regulation was regarded with some scepticism by a regulatory affairs manager, given the difficulty in predicting the future development path of an innovative technology and the likely inflexibility of the regulation that emerged from this process. Another issue raised related to the potential delay this approach would entail in the development of legally enforceable regulations, given potential risks to patients from cell therapies.

4.3 Industrial biotechnology / synthetic biology

4.3.1 Future products and their governance – interviewee perspectives

It is becoming increasingly clear that the regulatory precedents adopted globally for industrial biotechnology and synthetic biology will be those currently in place for GM technologies (Bar-Yam *et al.,* 2012). The products currently envisaged in these areas can be seen as incremental developments arising from GM technologies so this should be a logical and unproblematic choice, as is likely to be the case for countries such as the USA and Canada (Mittra *et al.,* 2014a). However,

in the EU, the GM regulatory system is seen as overly precautionary and politically influenced (Tait and Barker, 2011).

Recent changes in EU regulatory systems were seen by an interviewee to have potentially negative implications for synthetic biology. The relevant distinction is between an EU Regulation (with which all member states have to comply) and an EU Directive (where member states have flexibility as to how they meet the requirements of the Directive in their own national jurisdictions). The EU is moving away from Directives towards Regulations to minimise the number of different interpretations of a Directive in different countries. One interviewee claimed that the replacement of Directives 79/117/EEC and 91/414/EEC on crop protection products with Regulation EC 1107/2009[14] will require 20,000 to 40,000 pages of scientific reports to apply for a licence to operate. The scientific guidance documents that accompany such a regulation were described as 'parallel legislation'.

In the synthetic biology context, GM crops were a disruptive technology for the agrochemical industry sector that led in their development twenty years ago, but these companies have now accommodated their business models to the new technology and for them future synthetic biology related products are likely to be incremental in their impacts. For industrial biotechnology, synthetic biology will be partially disruptive, requiring radically new manufacturing processes (biological and fermentation based rather than chemical transformation of fossil fuel products) but there will be no disruptive changes in markets or in the regulation of the eventual products.

Standards related developments are playing a prominent role in innovative developments in this sector. One important requirement is convergence on standard terminology for the sector, developing a common language that will be needed in the development of future regulations. Industry should take a proactive approach in developing such standards that could either pre-empt regulation or set a more sensible reference range for the development of regulations.

Where GMOs are used to manufacture complex protein molecules, the current regulatory system makes it prohibitively expensive to change the organism used in production even if new, more efficient processes emerge and this is an area where new standards could allow greater flexibility to change the production system within the boundaries of standards protecting against health or environmental risks.

Most of the issues raised by industrial biotechnology come under the well-established, relatively uncontroversial regulatory system for contained use of GMOs. However, as the focus of innovation moves towards synthetic biology, proposals are being made to use biological containment (genetic firewalls) based on synthetic biology techniques to make such containment a more realistic proposition. This approach was seen as appropriate for risky activities requiring higher levels of containment of the relevant organisms as a fail-safe arrangement in the event of an accidental release. However, currently these techniques are being developed for very low risk organisms as 'proof of principle'. Based on past experience, there is a possibility that this work at low risk levels will come to be regarded as the minimum acceptable level of control, very considerably exceeding a proportionate degree of risk mitigation. This kind of over-reaction, a form of 'gold-plating' tends to arise where regulation is being developed as a PR exercise, to provide public reassurance and counter the excessively precautionary claims of advocacy groups.

[14] http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32009R1107

4.3.2 Relative roles and interactions of regulations, guidelines and standards.

For a company manager working in pharmaceuticals manufacture, using chemicals-based systems and now moving to industrial biotechnology based on synthetic biology, the field has always been heavily regulated with emphasis on guidelines and standards only where these are backed up by regulatory authority (e.g. a pharmacopoeia manufacturing standard).

However, in industrial biotechnology, although synthetic biology is currently a relatively small subset of the total company activity, the future potential of cell factories was seen to be enormous and operational standards were seen to have a very important role in these future developments, particularly standardisation of the metrology. However, so far the process of standardisation in this area was seen to have involved mainly using words, pictures and images from engineering to draw out a biological system, not adding anything new beyond a different way of expressing oneself. It was seen as important to think about what one is trying to measure in a biological system, given the potential interactions between DNA, RNA, proteins, and other chemicals. DNA is easy to measure; RNA is an order of magnitude more difficult but still possible, but from the point of view of developing a new manufacturing process the proteins (catalysts) are the most important to measure and standards need to relate to measurements that add value. (There can be a range of three to four orders of magnitude difference in the same system measured under different conditions.) The lack of standardisation in measurement was seen to be the biggest hold-up in the development of industrial biotechnology.

In the development of such standards, individual companies, industry groups or organisations were expected to develop their own standardisation first, potentially leading to a cross-industry set of standards. Academics were expected to have a role in standardisation of the nomenclature. However, if a company were to succeed in developing a standard process to deliver consistent manufacturing outcomes it is expected to be reluctant to share this with others, making it harder to develop a cross-industry standard as companies become more entrenched in working with their own systems. Key advances in enabling standardisation of manufacturing processes are expected to come from instrumentation, for example to measure the concentration, conformation and activity of a protein, including advances in the screening and measurement of phenotypes to indicate how different systems are interacting with one another.

In the industrial biotechnology community, there is nervousness about political issues arising from the association of synthetic biology with GM technologies, and the potential regulatory and political issues that may arise from these associations. Most procedures will be under contained use conditions, but the risk assessment process requires a consideration that there could be an unexpected release. With most of the organisms currently likely to be used in industrial biotechnology there are generally few problems, but in future there may be a need to work with organisms whose properties are not currently known.

4.3.3 Flexibility and adaptiveness of governance systems

For a policy maker who had worked at the international level in the early stages of GM regulation in Europe, the main objective of regulators at that point had been to allow marketing of GM products. There was no sense that these products presented risks that would warrant regulation, but rather a concern to use standards to control variety. Today there was acknowledged to be a clear need for a change of direction in Europe but a lack of leadership and an inability to change direction once the system has gone down a particular path. However, another interviewee understood that EU regulators are now experiencing ‘embarrassment’ about the way they have regulated agricultural biotechnology and this may help to avoid similar situations in future.

A regulator working in health and safety agreed with the proposition that a regulatory system will be difficult to adapt to changing circumstances including the emergence of innovative technologies. However, recently, the UK Health and Safety Executive adapted the Contained Use Regulations dating from 2000[15] for contained manufacturing processes using GMOs to make the process more *proportionate*, avoiding going beyond the requirements of EU Directive 2009/41/EC for low risk categories. This also involved changes to the relevant guidelines. However, following this move to a more proportionate approach, with potential savings for the organisations concerned, there has been virtually no adaptation and affected organisations have continued to apply the previous system.

The issue of organisations going beyond what the law requires may need to be addressed across the board for regulatory requirements. It may relate partly to the role of consultants with a potential vested interest in making the regulation more complicated than it needs to be. However, it also arises where the health and safety expert is employed directly by the organisation concerned. By going beyond what is required a regulator, policy maker or company manager is diminishing the value of a regulation when it is actually required. There is real value in proportionality.

There was a pronounced difference in the ability of companies working in this area to interact with regulators and standards bodies, compared to medical sectors. Company interviewees noted that there has been across-the-board removal of company expertise from committees advising European regulators and policy makers because of a deemed conflict of interest, for example in the work of the European Food Standards Agency (EFSA). Such conflict of interest charges are directed exclusively to industry, ignoring other sources of bias (e.g. political or religious) in other potential consultees. This process also excludes academic experts who may have had a previous association with industry, who are likely to be the only other group with scientific or technical expertise on a particular issue. There is thus a lack of technical expertise among those advising the regulators in GM-related areas.

Two initiatives from the European Risk Forum (a not-for-profit think tank set up by industry to promote high quality risk assessment and risk management decisions by EU institutions)[16] are seeking to address this problem:

- The Innovation Principle advocating consideration at every stage in a regulatory process of its impact on innovation; and
- The Law of Administrative Procedure, proposed to be included as a component of the Better Regulation Initiative[17].

These initiatives are intended to stimulate a cultural change through the innovation principle and a procedural change through the Law of Administrative Procedure.

The concept of working together through consensus to develop standards and guidelines was seen as excellent, but the current situation for pesticides and GMOs, where any involvement of industry is seen as a conflict of interest, was perceived to be unworkable. There are industry concerns that these problems will extend to nanotechnology and synthetic biology.

Considering the use of GMOs to manufacture complex protein molecules in industrial biotechnology, the current non-adaptive nature of the regulatory system makes it prohibitively expensive to change the organism used in production even if new, more efficient processes

[15] http://www.hse.gov.uk/biosafety/gmo/whats-new.htm
[16] http://www.riskforum.eu/
[17] http://ec.europa.eu/smart-regulation/index_en.htm

emerge. This leads companies to avoid moving to more efficient production systems because of the costs of amending the product licence. This was seen to be an area where development of standards could allow greater flexibility to change the production system, within the boundaries of protecting against health or safety risks.

The system of using standards and guidelines to give more detailed, prescriptive information about meeting health and safety requirements, while keeping the regulatory requirements at a more general level, was seen to fit well with the need to be adaptive to the emergence of new innovative technologies. Also where a new technology is emerging, one objective of regulation should be to make it simple and clear for small companies, to inform them on how they can comply with the regulation. The development of standards through BSI may be a useful way to approach this so long as it can be done without increasing the regulatory burden.

4.3.4 Issues related to disruptive and incremental innovation

An interviewee described the pressures on established companies to focus on incremental innovating in terms of making sure that your existing business keeps paying the bills through 'defensive R&D'. Synthetic biology is seen to be raising disruptive possibilities that were not imagined ten years ago but the regulatory environment in Europe is also seen as increasingly problematic. A better approach to regulation could be to consider the environmental goals we want to achieve rather than using prescriptive regulation to direct the process of getting there (regulating the outcomes, not the inputs). Such an incentive-based system could be used to demonstrate that a novel innovative technology will either have no impact on the target level of protection or could improve the level of protection.

In the early stages of development of a potentially disruptive technology, as is currently the case for synthetic biology where it is not yet clear how the technology will develop, premature imposition of standards and regulations was considered to risk constraining future developments. Once the direction of innovation becomes clearer standards and regulations become more relevant and applicable.

Another potentially disruptive change was seen to be the adoption of synthetic biology techniques to enable the manufacture of significant quantities of complex molecules that would not be viable today, one of the main bottlenecks in bringing many more advanced materials to the marketplace.

A regulator described how, when faced with an innovation that seems radically different, the tendency is to look for an existing regulatory system into which it could be accommodated, rather than developing a new regulatory system requiring a different model of thinking. In the case of synthetic biology, it is not yet clear to regulators whether it is just a more sophisticated version of genetic engineering or whether it will need another label and a different regulatory system.

4.4 Financial technology – FinTech

FinTech is being regulated under the current financial services system with overarching responsibility falling under the FCA, with a conscious effort to develop a regulatory system that does not unnecessarily hinder innovation. The challenge is to manage, for example, operational risk, trading risk, credit risk, reputational risk, payment risk, fraud and crime prevention, and systemic risk.

FinTech can disrupt the way financial services markets function in favour of consumers and supporting the efficiency of the market, and flexible and adaptive regulation of the sector is well understood to be important. The FinTech team in the FCA have consulted academia, industry (incumbents and FinTech firms), and other regulators on crafting a regulatory system that meets both consumer protection and competition objectives. As part of these efforts, Project Innovate

targets new and incumbent firms to support navigation of regulatory challenges. As part of supporting regulatory flexibility Project Innovate has set up a Regulatory Sandbox (FCA, 2015b), a safe environment for emerging innovative businesses to test innovations, business models and delivery mechanisms without incurring the normally high costs of compliance and regulation, given that new entrants are likely to be SMEs. Emerging questions include whether what is being regulated is a technology firm or a financial services organisation, and the advantages of principle based over prescriptive regulation. According to Black *et al.* (2007) "Principles-based regulation means moving away from reliance on detailed, prescriptive rules and relying more on high-level, broadly stated rules or principles to set the standards by which regulated firms must conduct business".

Respondents argued that it was important not to 'gold plate' regulation, a process that discriminates against SMEs and favours larger resource endowed organisations.

4.4.1 The governance challenge

Regulating the emerging Fintech sector is complex because operations span software, payments, data, platforms, and multiple financial service activities (Figure 3). The payments and peer to peer lending operations, credit reference, E-Wallets/prepaid cards of FinTech, and aggregators and quotation platforms, span consumer and wholesale banking and personal insurance (Ernst & Young (EY), 2014, p8). Products or services such as trading platforms, capital markets software and middle and back office software straddle asset management and capital markets (EY, 2014, p8).

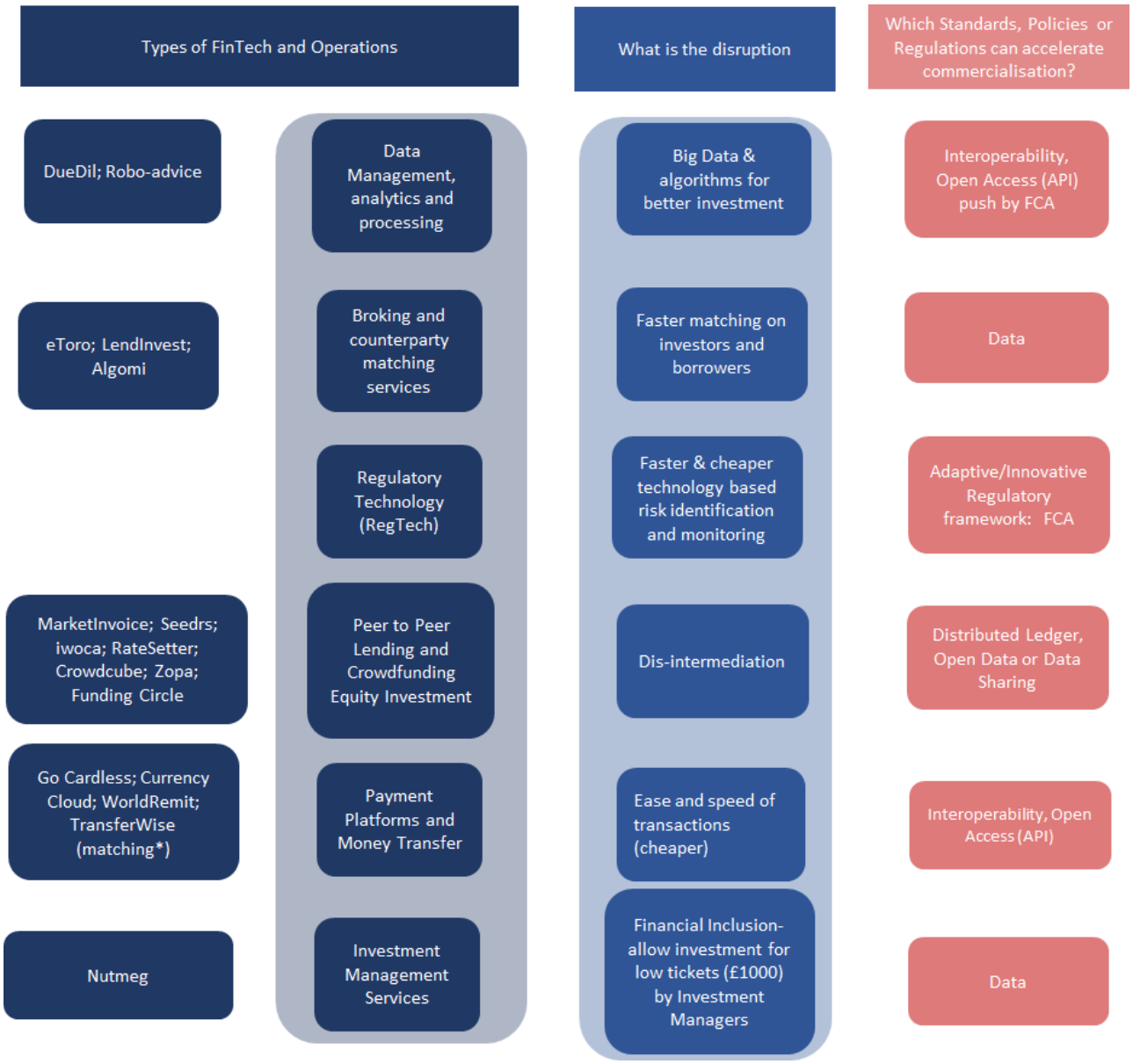
Interviewees suggested that mainstream financial services have difficulties dealing with innovation, especially innovation in FinTech, despite mainstream financial services being one of the biggest consumers of technology (ICT). Some mainstream financial services organisations have FinTech but they face challenges in on-boarding new products. The new innovators may have too narrow a scope because they solve problems they understand as consumers but do not fully understand the complexity of financial services governance.

In addition to managing risks and protecting the consumer there are systemic integration challenges between FinTech [SMEs] and mainstream financial services. Fintech needs access to bank accounts and bank systems, and standards are a key component of the integration, but their motivations may be divergent and power (in terms of information, systems and customers) is held mainly by mainstream financial services. Standards around compatibility and interoperability are critical and they should also addresses the use of technology for automated risk assessment - RegTech (regulation technology).

Outsourcing is an important issue in the financial services market, and regulators hold the regulated entity (financial services organisation) responsible for how third parties operate. There is a need for due diligence to be done on managers and directors of FinTech given that some of the operators are not financial services authorised firms but technology firms. The challenge is deciding whether they should be governed under normal rules and regulations of the FCA, and understanding whether what is being regulated is the technology or the business proposition. The FCA has initiatives (Project Finance: Innovation Hub/Regulatory Sandbox) to assist innovators in this regard.

The regulatory system can be either prescriptive or principle based regulation. Some argued that principle based regulation works well with organisations that have a healthy culture. For organisations with unhealthy cultures principle-based regulation becomes ineffective and has no effect in protecting financial services consumers.

Figure 3. Types of Fintech, their operations and the role of standards and regulations in accelerating successful innovation



4.4.2 Relative roles and interactions of regulations, guidelines and standards

Research evidence shows that the financial services sector is a moderate user of general standards such as those developed by BSI (CEBR, 2015). The sector also has industry-specific standards, for example the SWIFT (Society for Worldwide Interbank Financial Telecommunication) network. BSI standards used in the financial services sector fall into three categories: quality and operational risk management; good practice; and payments security and information (technical standards) (BSI, 2015); with data protection straddling the other standards.

There were divergent views among interviewees on whether standards can work with regulations and guidelines for FinTech and which should come first when little is known about the technology.

Standards employed in anti-money laundering came about through the JMLSG (Joint Money Laundering Steering Group) guidance on anti-money laundering which caused 'headaches' for the industry. The standards were employed in financial services, because they were generally invoked by the Government rather than by industry.

On the interaction of standards, guidelines and regulation key questions to ask are: what are the risks and issues in the market, and what are the appropriate protections or standards that need to be set? If the appropriate protection fell within the regulations, then standards cannot be a replacement. However, if what is under consideration is an emerging market or technology, for example virtual currencies where currently there is no regulation, one respondent suggested that standards would be appropriate to ensure integrity and safety, and to build trust amongst people so that the market or technology is able to flourish.

4.4.3 The role of standards in FinTech

A culture of collaboration amongst insurance players in London was highlighted as a key reason why the sector was globally leading in developing standards for the sector. A regulator said that the Treasury are in favour of using standards given what has happened with the credit market and how it was regulated. It moved from the Lending Standards Board, to OFT (Office of Fair Trading) and it is now with the FCA, and the standards are much higher. The cycle is similar for general insurance and mortgage governance.

An actor in the FinTech field remarked that designing a regulatory framework for an emerging technology like FinTech, and encouraging it, requires openness and transparency. Considering the culture it is also important to consider what other technical or mechanical instruments are needed to govern the sector. The sector could ask the BSI to coordinate development of standards, not necessarily because that would improve the governance but, by improving standards, they would simplify the process of regulation or automation. Creating standards simplifies the process globally making it cost-effective, and minimising operational risk. There is a need for actors to collaborate on a common set of standards that are mutually beneficial and backed by the industry.

The UK Government is encouraging competition in the financial services sector by calling for an Open Standard API (Application Programming Interface) and by encouraging incumbent financial institutions to open up their systems to innovative new entrants for data analytics and management and regulatory technology (RegTech) to deliver, for example, regulatory compliance (FCA, 2015a). In this instance regulators are using standards as a tool to integrate the two parties and reduce transaction costs by decreasing platforms for interconnectivity[18].

4.4.4 Issues for disruptive and incremental innovation

Regulators in financial services are beginning to develop expertise across the sector and where they do not have the expertise they draw on other parts of the FCA. Regulators have set up a one stop shop for all firms to draw together intelligence on what is happening across the market. Regulators are considering the concept of 'proportionate' regulation for emerging technologies thereby recognising the special circumstances of SMEs in the FinTech area. The FCA can give individual guidance which is specific to a business about how its business model works in a specific circumstance. They also give general guidance to the whole market which firms can rely on.

[18] http://www.ukfintech.com/security-regulation/open-standard-api-will-benefit-the-innovators

4.4.5 Testing environment

Regulators in financial services are drawing lessons from the clinical trials area to develop a 'clinical testing framework'. However, they realise that juxtaposing the pharmaceutical clinical testing environment with financial services without due consideration could carry over redundancies and challenges experienced in medicines governance systems in a way that would not benefit the financial sector. The regulators will decide for every case what constitutes a satisfactory testing environment, and interviewees acknowledged that the biggest challenge would be the concept of a representative sample for a trial which seems inappropriate for FinTech. The regulator recognised that incumbents (big companies) favour heavy regulation, because it acts as an entry barrier for smaller competitors. For example if virtual currencies were regulated in terms of the basic level of FCA standards only a few players would remain and this would run contrary to the competition imperative for the FCA.

4.4.6 Regulatory flexibility

The financial services regulatory authorities show evidence of building regulatory flexibility into their approach to regulating the FinTech sector. The Innovation Hub was set up because the FCA saw both opportunities and risks in innovation. The opportunity was that FinTech can disrupt the way the financial services markets function for the good of consumers and for the efficiency of the market.

Project Innovate targets innovative new firms and those already in the market and assists them to navigate regulatory challenges. An example of regulatory flexibility under Project Innovate is the Regulatory Sandbox concept (FCA, 2015b), a safe environment for emerging innovative businesses to test innovations, business models and delivery mechanisms without incurring the normally high costs of compliance and regulation, given that new entrants are likely to be SMEs.

4.5 Sector-related differences

The choice of case studies for this project has enabled us to understand better how the histories of different sectors, particularly the nature of the governance processes that have emerged over the past fifty years, have shaped their innovation potential.

- *Personalised medicine manufacture*: regulation for this area of innovation is located within the pharmaceuticals sector, with one of the most demanding regulatory systems in terms of financial cost and time required. The case for regulatory adaptation to enable more innovative products to be developed has been pursued for over ten years (Chataway *et al.,* 2006; Tait *et al.,* 2007) and there are now several initiatives that could be described as regulatory adaptation in the direction of greater proportionality. Most important, from our interviews, a common perception was that regulators and companies are now able to have very useful dialogue on the nature of the regulatory systems and which adaptations could be managed most easily by the companies involved. Some questions were raised about the extent of *real* adaptation that is forthcoming, but on the whole, the involvement of industry was closer to what has been described as part of a standards-setting process, rather than for the traditionally arms-length regulatory approach.
- *Industrial biotechnology/synthetic biology*: this sector is likely to be governed by the regulatory process that has emerged in the EU for GMOs, a process that is as demanding as that for pharmaceuticals, but also subject to a political overlay that can have very perverse outcomes for innovative technologies. Here, the case for regulatory adaptation to accommodate safely new innovative technologies has not been made at the EU level,

although the UK government has proposed useful initiatives. The most optimistic projections are that the current regulatory system for GMOs will be applied to these new areas with no further ratcheting up of regulatory requirements. However, overall, 'no change' seems to be the best that can be expected. It is also notable that company interviewees generally perceived interactions with regulators to be few and difficult, leaving no counterbalance to the influence of green advocacy groups, and making it difficult for any collaborative approach to the development of standards or regulatory guidelines to emerge. In a small but potentially significant move counter to this trend, a concerted effort has been made by the UK Health and Safety Executive to remove 'gold-plating' of the regulatory system for GMOs in contained use.

These very different sectoral backgrounds point to the need for sector-specific approaches to devising future roles for standards in the overall governance process and, for any future research, careful consideration of which areas are most important to address in future, and which are likely to be most amenable to new approaches to the roles of standards in governance of innovation.

4.6 Expertise-related differences in perspectives

Within each of the sectoral case studies, interviewees had different perceptions of the potential roles of standards in the overall governance process. Industry contacts were very familiar with the standards process, whereas lawyers working in regulatory areas had less contact with it. Company regulatory affairs managers in health related areas generally relied on regulations and regulatory guidelines/pharmacopoeia standards (carrying equivalent authority to regulatory guidelines). Consultants working in regulatory contexts also seemed to have less engagement with standards. Industrial biotechnology interviewees were very familiar with standards, as they applied to manufacturing processes.

Generally speaking the standards referred to by interviewees were those that dealt with production, manufacturing, quality and safety for well-established processes, rather than their use in the early stages of development of disruptive innovation, but this latter approach to standards development was seen as potentially interesting and was more in evidence in the FinTech area.

From a legal point of view, in the regenerative medicine area, there were references to cases where a regulation had been applied in a manner which exceeded its legal mandate, a form of 'mission creep' or 'regulatory creep' that occurs particularly where novel technologies are involved. The subsequent legal battles can mean that particular innovations are never developed. Controlling such actions by regulators should be part of the overall governance process. Another example is the development of autologous cell therapies where the regulatory intention from the earliest stages of development was to treat them as equivalent to allogeneic therapies (i.e. through the pharmaceutical regulatory system), and this has raised problems for the current development of such therapies. There have also been several erratic decisions by scientific advisers and regulators that can in the long run lead to important inconsistencies in interpretation of the law. Solutions for some of these problems could be:

- To regulate medical practice through the development of standards for best practice; and/or
- To standardise human cell types and tissue types, on a scientific basis, according to their essential functions, through a Framework standard, supported by a vocabulary standard to define 'essential functions'.

4.7 Stakeholder workshop

A stakeholder workshop on *Effective Governance of Emerging Technologies,* held to discuss the outcomes of this project, attracted 36 stakeholders representing industry, policy and regulatory bodies, government departments, academia, consultants, and consumers. Following presentations from the BSI and the Innogen Institute, general interactive sessions discussed the roles of regulations and standards in governing emerging innovative technologies, key concerns from the stakeholder perspectives and the value of the proposed Governance Framework for Emerging Technologies. Breakout group sessions were held to allow participants to explore issues specific to the three case studies for this project.

The following sections provide a brief summary of the main points raised by stakeholders in discussions. Overall there was agreement that the framework proposed here was feasible, useful and indeed is already in operation in some areas of governance of innovative technologies. For example, there was reference to the extent to which, in medical areas of regulation, there is already fruitful interaction between innovators and regulators. However, some stakeholders questioned whether this was working as well as regulators thought.

The following summary points from discussions focus particularly on *additional* points made in discussion that are not already covered in Sections 4.1 – 4.6.

4.7.1 Comparing standards and regulation

When are standards the best approach?

- Standards and guidelines have an adaptive aspect in their development. Guidelines are live documents and they can be changed as new knowledge is generated as regulators interact with industry.
- Standards have three benefits for government: they are a cheaper alternative to regulation, they can be a precursor to regulation, and they can lead to market acceptance.
- If the technology changes standards can be more easily updated than other governance tools.
- Standards can be helpful in the early stages of developing a technology:
    - When setting up core principles and standardising terminology;
    - For validation of core technologies to give better quality processes;
    - When you cannot speculate on the end point of a technology and want to encourage as many innovation pathways as possible;
    - When guiding the process for innovators.
- When being aspirational and you want to get to an endpoint without the government or a regulator coming in too early.
- Carrying out tests or trials, for example self-driving cars
- Encouraging interoperability.
- When you want to bring in stakeholders and build public awareness (but it is important to consider who chooses relevant stakeholders?)
- Transferring knowledge between sectors.

When is regulation the best approach?

- When there is a need to manage a potentially severe impact on society or to ensure safety, to ensure compliance.
- When there is a need to control access to a market.
- When there is a need to regulate or manage risks.

- To deliver innovative outcomes through the use of regulation, for example the Building Information Management System in the construction sector.
- Where regulation needs to be linked to testing standards, as in vehicle pollution standards.

4.7.2 Comments on the Innogen Framework

A flexible approach to govern technology that does not stop alternative development pathways was seen to be helpful, and stakeholders generally liked the idea of using standards in early stages, leading on to development of guidelines and eventually regulations. The role of standards was expected to be different in the early innovation stages (possibly focusing on terminology) compared to later development and marketing stages. At points close to the marketing stage standards could be useful for SMEs in gaining access to finance.

The following additional points were seen as useful to consider:

- Can one predetermine when to use standards, guidelines or regulations?
- Demonstrating that the firm has control of the process is important to regulators.
- In encouraging interaction between regulators and innovators it is important to ensure that regulators keep enough distance to remain objective in their assessments - they have been criticised for being too close.
- There may be more than one regulator involved for a technology and it is important to understand (i) which regulatory system has the biggest impact on innovation and (ii) the effect of a combination of different regulatory systems.
- There is a need to consider who the relevant stakeholders are and how do get them involved. It is also important to involve users, consumers and patients to understand issues of affordability, accessibility and usability.

4.7.3 Personalised medicines: autologous cell therapies

A stakeholder made the point that in practice in the medicines area nothing has changed in terms of regulation (statutory changes); most of it has been dealt with through guidance and standards, with a lot of consultations and iteration as different products have come through the regulatory process. The EC process, beginning with directives and regulations which are then supported by guidelines is a flexible system. Standards should particularly be looked at for research being done in universities.

In the manufacturing area there was seen to be a place for standards in, for example, platform validation for very complex high throughput processes.

A regulator described the 'fellow traveller' concept as follows:

- When there is something new, and there are different degrees of newness, the regulators ask that the innovator tells them about it so that they learn more about it.
- The innovator then becomes more confident with go or no go decisions.
- Following a series of meetings at different times and eventually the dialogue becomes scientific advice.

Another example was given where regulation of rDNA was guideline driven:

- When the technology came in the 1980s there was no regulatory precedent
- Regulators sat with innovators and developed guidelines
- These guidelines were developed over several years and helped rDNA products to come through.

In contrast, for ATMPs in Europe:

- Industry wanted to know which path they should take to develop a product.
- Regulators drafted a very general regulation with the intention of it not being restrictive but to depend on the next level down – guidelines that could be readily be changed to avoid inhibiting the development of the product.

Regulators were described as being reluctant to go down the chemical route when regulating some technologies, asking whether the approach is fit for purpose, for example with transplantation within a patient in the area of oncology and immunotherapy.

Evaluation standards for diagnostic tests were seen to be an area that has not been covered well to date.

4.7.4 Industrial biotechnology/synthetic biology

This discussion considered nomenclature and definitions, seen to be important in developing regulation for the sector, involving consideration of standards. An alternative could be to start with standards as a way of generating definitions.

- For emerging technologies there are challenges related to risk perception creating a need to distinguish between plausible and speculative risks when dealing with emerging technologies.
- If we start thinking of governance early then which governance tool is relevant to deploy in the development stages of an emerging technology?

4.7.5 FinTech

Considering key issues when governing new technologies, the discussion focused on the example of digital currencies to identify the issues. Questions and issues considered included:

- How do you make something that people don't understand trustworthy? There is a need to make a distinction between the technology itself and who to trust. There is nervousness around the technology and the business model underpinning it, and who props it up if it fails.
- There is layering of technology in terms of the backbone of the internet and the bitcoin technology. The blockchain system may be fantastic but if the underlying backbone system is not solid then there are challenges.
- High level standards developed by the industry for blockchain need to come in early in the process of development of the innovation and its application to FinTech and the financial services.
- Indemnity consent forms given to consumers on FinTech assumes the consumer is sufficiently financially literate to participate in the market.
- Apart from bitcoin, blockchain can be used in any part of financial services and can create change in back office operations, resulting in reduction in transactional costs.
- The Innogen framework makes sense for technologies like block chain because no one yet knows the evolutionary pathways for the technology and innovation.

5. Conclusions: a governance framework for innovative technologies

5.1 Rationale for the framework

The overall theme of this project, "… the role of standards and regulation in unlocking successful innovation in a way that accelerates technology commercialisation without leading to undesired outcomes" can be seen as an important contribution to the work of a number of regulatory agencies and policy bodies in developing more proportionate and adaptive approaches to the governance of innovative technologies, as noted in Sections 1 - 3. The focus on proportionality arises from a sense that current EU regulatory systems, as they have evolved since the 1970s and as they have dealt with the emergence of new innovative technologies, have become unnecessarily rigid and difficult to adapt to changing circumstances. This project has explored a role for the creative and targeted involvement of standards in the process of developing more proportionate and adaptive governance systems for future innovative technologies across a range of business sectors.

The broad conclusion from this report is that there is at present no overall framework to guide decisions by regulators, policy makers and standards bodies on the appropriate mix of standards, guidelines and regulations in governing different technologies at different stages in their development. The Governance Framework proposed here (Figure 4) envisages an approach to judging how to deliver proportionate and adaptive governance of innovative technologies for different degrees and types of innovation, across different industry sectors with widely differing histories and experiences of regulation. It could potentially unlock greater commercial potential from emerging technologies while also addressing regulatory and public concerns about risk, safety, quality and efficacy.

The framework picks up on the main issues raised in our introductory sections and also in the discussions with interviewees and stakeholders, particularly the overarching point about the need for governance systems (including regulations, guidelines and standards) to be more proportionate and adaptive than they are at present:

- Current governance systems for innovative technologies lack coherence and are in need of an approach like the one proposed here to guide more effective decision making.
- Different governance approaches will be required for disruptive and incremental innovation.
- The relevant elements of a governance approach that will need to be addressed will differ across sectors, as exemplified by the three case studies.
- It is a relatively common experience that where a regulatory system is imposed in the early stages of development of an innovative technology, it requires subsequent adaptation but proves difficult to adapt.
- Where guidelines and standards exceed the minimum requirements of a regulation or go beyond reasonable societal expectations for political reasons ('gold plating') this can have serious negative impacts on innovation.
- Where standards are employed with the intention to reduce variety, this may lead to different outcomes for disruptive and incremental innovation. For an incremental innovation, reduction of variety can help to create viable markets. In the early stages of development of a disruptive innovation, it may be desirable to retain as much variety as possible until it becomes clear what the winning technology will be.

- No general conclusions can be drawn on whether standards or regulations/guidelines are more consultative with stakeholders during their development – there is considerable variation across sectors. However, there will be inevitable differences in style and outcome where the regulator is in charge (regulations/guidelines) and where industry takes the leading role (standards).

There are important differences in the policy environment experienced for different sectors, for example comparing cell therapies, synthetic biology and FinTech.

- Innovation in personalised medicine manufacture for autologous cell therapies is disruptive at all levels (scientific research and early development phases, manufacturing and translational development, and at the market level where it will, if effective, undermine some of the markets of multinational pharmaceutical companies). Other sector specific factors include:
    - Difficulties experienced in adapting a chemicals-based regulatory system to govern biological products;
    - The need to protect patients from harmful procedures using a clinical trial-related process enshrined in regulation;
    - Difficulties in developing standards and guidelines for cell manufacture;
    - Absence of a governance system for some cell therapy applications;
    - Different expertise-related perceptions of the openness of the regulators to desirable adaptation of regulatory systems;
    - The European Pharmacopoeia standards (equivalent to guidelines) perform an important role in medical regulatory systems, including cell therapies, but the system was criticised by some as being expensive and bureaucratic, and sometimes duplicating standards developed by others;
    - The competitive nature of the industry and difficulty in persuading companies to collaborate, e.g. to develop a consensus standard, and risks to patients caused by the delays this might entail.
- Industrial biotechnology/synthetic biology innovation can be seen mainly as incremental, building on the now-routine development of GM-related technologies, at least for countries outwith the sphere of influence of the EU. Relative to GM technologies, industrial biotechnology is incremental at the research and early development stage and at the final marketing stage where the manufacturing companies will mainly be using the new techniques to replace the chemicals-based manufacturing processes, delivering to existing markets. However, replacing the manufacturing process will be a disruptive change for the industrial biotechnology companies concerned, requiring new facilities and new skills in the workforce. Additional relevant sector specific issues include:
    - The choice of GM regulatory systems as the precedent for these technologies should be unproblematic, except for the dysfunctional nature of the EU regulatory system. This leads to pressure for adaptation of the EU regulatory system, so far to no effect.
    - Standards are playing an important role in developments in synthetic biology, for example to develop a common language that will be needed for the development of any future guidelines or regulations.

- There is a need for adaptation in the regulatory systems in place for the manufacture of complex protein molecules where it is prohibitively expensive to change the organism used in manufacture even if new more efficient processes have been developed; this was seen as a potentially useful area to use standards to initiate adaptation.
- Some proposals to use biological containment as a risk mitigation measure for relatively safe organisms used in industrial processes will amount to 'gold-plating', will be difficult to adapt in future, and could make these techniques less useful where they are needed for hazardous organisms.
- Given the enormous potential of cell factories, for example to enable manufacture of complex molecules that would otherwise be prohibitively expensive of impossible to make, the process of standardisation to facilitate innovation is moving too slowly and is too much focused on words, pictures and images; the most important challenge is to develop measurement standards for proteins.
- It will be important not to impose standards and guidelines prematurely so as to avoid constraining innovation; it is better to wait till the direction of innovation becomes clear.
- There was nervousness about political issues stemming from an association between synthetic biology and GM technologies.
- Interviewees working in this area found it very difficult to engage with regulators in attempting to meet the requirements of current regulations or in discussing future regulatory initiatives or adaptation, unlike the situation in medicine-related sectors.

- Innovation in the FinTech sector was likely to be disruptive at all stages of the innovation process (basic research and early development phases, translational development, and at the market level), for example disrupting the way financial services markets operate to make them more efficient for the benefit of consumers. However in this case the regulatory environment for the technologies likely to be displaced by it is very different, and the relevant risks are financial and reputational. Relevant sector-specific issues are:
  - There was a strong appreciation of the potential benefits of FinTech among financial sector regulators and a much stronger emphasis in their interactions with innovators on the need to avoid inhibiting FinTech innovation and to support SMEs working in the area.
  - There was a focus on 'Principle-based' rather that 'Prescriptive' regulation implying a move away from detailed, prescriptive rules towards high-level, broadly stated rules or principles as a basis for setting standards for regulated firms in conducting their business. (The case was made that principle based regulation only works well with organisations that have a healthy culture.) Using this language to describe regulation seems to be common in financial circles, but not in other sectors.
  - Mainstream financial services find it difficult to deal with FinTech, but FinTech needs access to bank accounts and bank systems and standards will be a key component of the integration.
  - Important types of standard will be around compatibility, interoperability and the use of technology for automated risk assessment (RegTech).
  - The regulator is alert to the fact that big companies favour heavy regulation as it acts as a barrier to entry – if virtual currencies were regulated through basic FCA

standards, a few large companies would dominate the scene, going against the competition imperative for the FCA.
- A range of projects is specifically targeted to assisting new firms to navigate regulatory challenges, e.g. the Regulatory Sandbox.

5.2 Framework for proportionate and adaptive governance of innovative technologies

5.2.1 Introducing the framework

Our proposed framework (Figure 4), builds upon the Innogen Institute research framework described in Section 2.1 and Figure 1. It summarises a way of conceptualising the relevant roles of standards, guidelines and regulations (as distinguished in Figure 2) and is proposed as a support for companies, regulators and policy makers in governing new emerging technologies across a range of sectors.

The green arrow on the left of Figure 4 represents the value chain that is central to Figure 1. The rest of the diagram explains in more detail how the elements of the innovation ecosystem that have been addressed in this project could be adopted in different ways at different stages in the innovation process, and for different types of innovative technology, to facilitate more proportionate and adaptive governance.

At various stages along the development of the value chain, from 'Early Stage R&D', through early and later stages of 'Translational Development', to 'Marketing', standards, guidelines and regulations will play different roles, and some may not need to be involved at all at some stages. Standards, guidelines and regulations, as shown in the central portion of the diagram, are categorised somewhat simplistically as 'soft', 'firm' and 'hard' law[19], and where human and environmental hazards are involved, the governance system will move closer to hard law (formal regulation) as the product reaches market-readiness. The standards and guidelines at the bottom of the chain are those that will support firms in compliance with the regulatory system, for example to ensure quality and safety of products, or good manufacturing practice. The broken line under guidelines in the central part of the diagram indicates that, for some technologies, relatively firm guidelines may prove a sufficient basis for governance with no need to move to a legally based regulatory system. Some aspects of FinTech may be in this category.

Interviewees and stakeholders were generally in favour of couching legally binding regulations in very general terms, and including detailed procedures, specifications and expectations in the guidelines and standards that are subservient to the regulations (bottom of Figure 4). However, given the varied nature of the governance challenges raised by innovative technologies and of the governance systems already in operation, any framework proposed to support decision making in these areas will itself need to be adaptive to future developments in innovation and policy.

For example, to summarise how proportionality could be achieved for a disruptive innovation for which there is no existing regulatory precedent, interviewees generally agreed with our proposed approach as embodied in the framework:

(i) In the earliest stage of developing the technology, focus on PAS and consensus standards devised in collaboration with companies and scientists with expertise in the area;
(ii) As experience is gained and the likely future nature of the emerging innovative products and processes becomes clarified, adapt the initial standards and begin to formalise them as

[19] Hard law has government based legislative enforcement to ensure compliance; soft law has no formal legislative authority but relies on codes of conduct reinforced by peer pressure or (for some standards) through market related mechanisms.

guidelines that could then form the basis of a future regulatory system (this stage involving companies and scientists and also regulators and policy makers);

(iii) Based on the guidelines, in an openly democratic process involving all interested stakeholders, develop legally binding regulations, couched in general terms relating to the desired outcome of the regulation; and

(iv) Also in an open democratic process involving all interested stakeholders, devise standards and guidelines to support compliance by those engaged in developing the new technology.

For incremental innovation there will be a continuing need for guidelines and standards to support innovators in compliance with current regulatory systems. An example of the power of adaptation of guidelines arose in the development of new anti-microbial drugs, where a change in regulatory guidelines for the conduct of clinical trials had a dramatic impact on innovation-related incentives, potentially reducing the cost of developing a new antimicrobial by 50% (Tait, *et al.,* 2014).

5.2.2 Disruptive and incremental innovation

Where an innovation is potentially disruptive across all points of the value chain (for example cell therapies), it is particularly important to ensure that the regulatory system and guidelines developed for its governance are proportionate to the benefits and hazards. We are proposing that an effective way to help to deliver proportionality could be, as outlined above in Section 5.2.1, to convene stakeholders to consider how standards could be developed from the earliest stages of R&D for the innovation, perhaps of the PAS type initially and then progressing to a consensus standard. As more is learned about the technology and its properties and potential in the early translational stage of development these standards can be firmed up as guidelines and will then, if necessary, provide the basis for a formal regulatory system. Given that they will have been developed from a standards-based consensus process with industry leadership, the resulting regulations are more likely to be proportionate to the needs and properties of the technology than if the process had begun with the development of new regulations or the designation of a particular regulatory precedent for the new technology. However, this process would need to be fast enough to ensure the protection of patients being administered the new procedure.

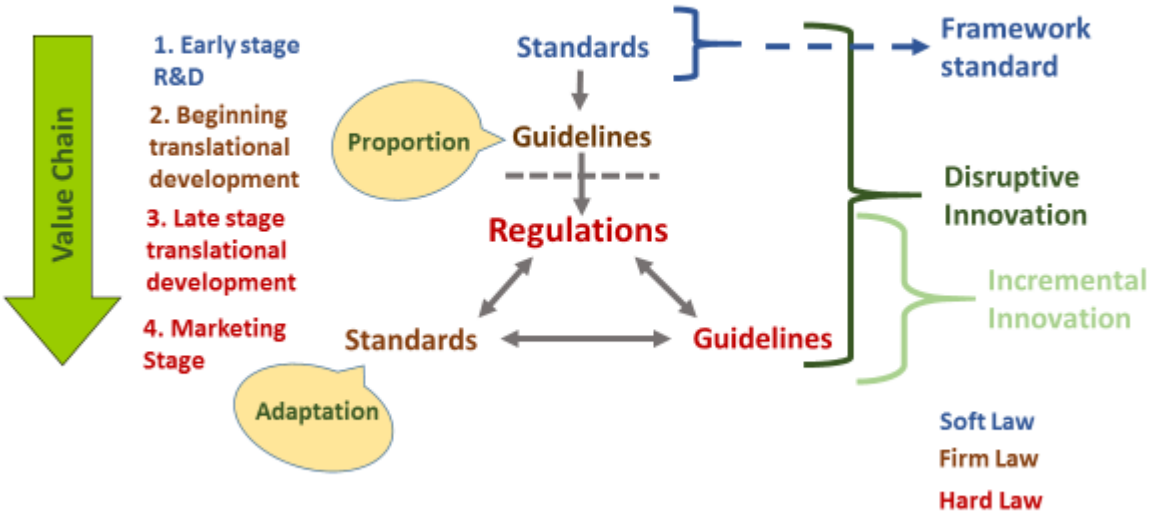
For an incremental innovation with a clearly-defined role in an existing value chain, an appropriate regulatory system with supporting guidelines and standards will probably already be in place, as indicated on the right hand side of Figure 4. However, as was described in the industrial biotechnology case study, for new manufacturing processes (Stage 2, Beginning Translational Development in the value chain) some aspects of the regulatory system in place may require adaptation to the requirements of the innovative process, and the use of consensus standards to adapt how the regulatory system deals with the new technology may be the most appropriate course of action.

5.2.3 Support for collaborating companies

To flesh out the simplified diagram of the value chain in Figure 1, consider the examples of a company outsourcing the manufacturing process for a complex drug molecule to an industrial biotechnology company; or a company or a not-for-profit organisation developing an autologous cell therapy outsourcing the development of a device needed to deliver the therapy; or a devices company developing a diagnostic tool to support the development of a new antimicrobial drug. In each of these examples, the two companies with their different business models will be subject to different regulatory and standards jurisdictions. A responsible approach to regulation would involve interaction between the relevant regulators or standards bodies to support co-development of the innovation and synchronisation of the business models. However, we are not aware of any examples where such integration has been undertaken by a regulatory body with the

intent to support innovation (Mittra and Tait, 2012; Tait *et al.,* 2014). It is easier to envisage joint consideration of the governance needs of collaborating companies being undertaken through the consensus process of a standards body, at least in the initial stages.

Figure 4. Framework for proportionate and adaptive governance of innovative technologies



5.2.4 Delivering proportion and adaptation

This framework is intended to support the delivery of two important policy objectives relevant to enabling innovative technologies to contribute more effectively to national and global economies, proportion and adaptation in governance systems (Section 1.1 and 1.2). As indicated in Figure 4, proportionality can be delivered most effectively if built into the regulations from their earliest stages of development and the suggestion to build from standards to guidelines and then to regulations could be an effective means to deliver this objective. On the other hand the role of standards in adaptation of existing regulations and guidelines to the needs of an innovative technology after they are in place is illustrated at the bottom of Figure 4; a consensus standards approach here could be a valuable aid to delivering adaptation. In both cases, the building of consensus would need to include regulators among the stakeholders involved.

5.2.5 Use of the framework

To summarise, we envisage different, but equally valuable, roles for standards and guidelines (as specified above), in contributing to proportionate and adaptive regulation of innovative technologies, both disruptive and incremental. However, further research will be needed to explore how these roles should be developed in different sectoral contexts and in collaboration with different sets of actors.

To give an example of how this approach might operate, in Section 4.3.1 an interviewee noted that, where potentially disruptive innovation based on synthetic biology is being fitted into an existing governance approach, there is a potential for early stage research on bio-containment as a control measure to be applied across the board as a form of ‘gold plating’. This may be an opportunity to develop a system of standards for bio-containment, to guide innovators on the

proportionate level of containment in the context of specific risks. Relevant considerations would be: what is a sufficient level of bio-containment for the innovation being discussed; and how reliable does it need to be in different contexts. A *proportionate* approach in such cases might be: (1) no biocontainment needed for Category 1[20] organisms in physically contained or uncontained use; (2) no bio-containment needed for Category 2 organisms in physically contained use (as is currently the case), and consideration whether some level of bio-containment is needed for deliberate release of Category 2 GMOs and therefore development of standards for such cases. Use of Category 3 and 4 microorganisms is assumed to be undertaken in physically contained conditions and bio-containment could have an important role as a fail-safe measure to provide multiple layers of protection between the hazard and an accidental release. Again there is a potential role for standards to ensure that the level of bio-containment required is proportionate to the risk and does not impose unnecessary costs on researchers and innovators. In the most hazardous cases, biological containment can involve multiple, orthogonal modifications that work in different ways and these should be considered from the point of view of a proportionate level of protection and not 'because we can'.

5.3 Responsible research and innovation

Given the potential impact of the UK and EU RRI policy agendas on companies developing innovative technologies (Section 1.2), the industry sectors to which it will be applied have a legitimate role to play in its development. However, this process has not yet begun in any formal sense. The development of a framework consensus standard is proposed here as an appropriate mechanism to address this policy gap (Figure 4).

RRI did not feature highly in discussions with interviewees although the concept of 'social responsibility' and the relevant standard (ISO 26000) was well understood. However, it was raised by stakeholders in the workshop, emphasising the importance of stakeholder involvement at all stages in the governance process described in Figure 4. RRI was familiar to those working in synthetic biology where it has already been widely discussed, but there was frustration that the emphasis on RRI for synthetic biology, to the exclusion of other industry sectors, implied (erroneously) that this sector entailed greater hazards than other comparable technologies.

The expectations of those currently involved in developing an RRI approach in the EU include:

- soliciting, listening and responding to stakeholder and wider public interests, hopes and fears;
- recognising that approaches to solving particular challenges should always be placed in the context of alternative ways of addressing the same problems (for example recognising that tackling world hunger or seeking to mitigate climate change are social and political challenges, to which technologies may contribute but need not have the leading role);
- considering who should be allowed to determine what is in the public interest; and
- getting answers to such questions before embarking seriously on development of innovative technologies.

These RRI-related pressures are real and cannot be ignored. However, there is a need for such pressures to be moderated by a better understanding of current governance systems, including the roles of standards and guidelines, how they operate now and could operate in future to shape industry sectors and to determine the range of innovative developments that can be delivered;

[20] Categories 1 – 4 in containment of organisms range from 'no foreseen hazard' at category 1 (organisms 'generally recognised as safe' (GRAS), to the most hazardous infectious agents at Category 4.

and the reasoning behind pressures for regulatory systems to be more adaptive and proportionate.

5.4 Future developments of the proposed governance framework

5.4.1 Achieving 'proof of concept' status for the proposed framework

Sections 4 and 5.2 have demonstrated how the proposed framework could contribute to the development of more proportionate and adaptive governance of innovative technologies in three very diverse case studies, autologous cell therapies, industrial biotechnology/synthetic biology, and FinTech. These case studies were chosen to demonstrate how different approaches are needed in the context of: different industry sectors with very different value chains; disruptive and incremental innovation; adaptation of existing regulatory systems in the context of innovative technologies; consideration of appropriate regulatory precedents for innovative technologies; and different regulatory cultures in different sectors. We have demonstrated, within the resource limitations of the project, that the proposed Governance Framework can be applied in a way that is capable of covering all these variations.

If this approach is seen to be sufficiently promising, there will be a need to explore its potential usefulness further, building on the three existing case studies and covering a broader range of innovative technology sectors, including additional key actors, and where appropriate considering the economic benefits that could accrue from implementation of this approach.

Additional target areas (not a comprehensive list) could be:

- new approaches to the development of pharmaceuticals in the context of the failing blockbuster drug value chains, for example developing new antimicrobial drugs to meet the antimicrobial resistance problem;
- the development of novel diagnostic tools, particularly in the context of stratified or personalised medicines;
- new plant and microbial biotechnologies with a potential to deliver a range of contributions including: nutraceuticals and other novel foods, pharmaceutical products such as vaccines, feedstocks for other industry sectors from food production to perfumes and flavours;
- biological pesticides;
- unconventional fuels; and/or
- robotics

Our interviews showed that learning across sectors is complicated by differences in terminology to describe similar types of standard, guideline or regulation, alongside the adoption of new terms to describe existing types of standard, accompanied by a lack of clear definitions. The proposed Framework could support the kind of cross-sectoral 'tidying up' that would help to clarify the roles of different types of standard and guideline in supporting and controlling innovative developments.

5.4.2 Impact of an innovation mandate

In the UK and the EU there is a range of initiatives designed to focus the attention of regulators on the need to support innovation as a contribution to national and regional prosperity and competitiveness (e.g. the EU Better Regulation Initiative[21]). This has resonated well with the agendas of innovators and regulators working in health and FinTech related areas but has had

[21] http://ec.europa.eu/smart-regulation/index_en.htm

much less influence on the industrial biotechnology/synthetic biology area. These circumstances would warrant further research on the extent of the success of an innovation mandate in areas where it does appear to be influential, and the reasons for lack of success in other areas. For both types of outcome there is an opportunity for further investigation on context-specific mechanisms to facilitate such adaptation, including a potential role for standards.

5.4.3 A new approach to RRI

As shown in Sections 1.2 and 5.3, there is a need for a more integrated approach to incorporating RRI (as desired by a range of stakeholders and citizens) within the overall approach to governance of innovative technologies. Stakeholder concerns are most likely to focus on innovations considered disruptive (and therefore most potentially valuable to the economy and society) and so that would be a useful starting point for development of this proposed approach.

The governance approach outlined in Figure 4 provides an opening for development of a Framework standard, beginning in the earliest stages of R&D, which takes into consideration the type of stakeholder dialogue that would be appropriate at different stages in the development of an innovative technology. For example the RRI approach outlined in Section 5.3 currently entails no concessions to proportionality or adaptation – it does not seem proportionate to insist on exploring alternative ways to solve the problems of world hunger or global climate change before embarking on the development of an innovative technology. The Nuffield Council on Biotechnology in its report on *Biofuels: ethical issues* (NCOB, 2011), concluded that, if a novel biofuel could be produced in accordance with a standard set of ethical principles, and if it could contribute to mitigating global climate change, then there was an ethical duty to develop it (within the constraints of technical and commercial feasibility). Such dialogue initiatives are expensive and time consuming and can feasibly be conducted on a class-by-class basis for novel technologies, but it would not be appropriate to engage in such a dialogue for individual innovative developments within a general class. This is where development of a framework standard could have an important role to play.

5.4.4 Who needs to be responsible?

It is notable that, throughout all discussions and recommendations on RRI, the focus is entirely on the need for scientists and innovators to behave responsibly. Based on the ethical principle of equitable treatment of all stakeholders, the field is open for a new approach to RRI that also includes the desirability of responsible behaviour by regulators/policy makers (e.g. in being proportionate and adaptive in their regulatory decisions) (Lowrie and Tait, 2011) and by other stakeholders and citizens (in engaging 'responsibly' with other stakeholders) (Tait, 2009). The Innogen Institute has begun the process of developing guidelines for Adaptive Governance of Innovative Technologies (AGIT) and for Constructive Stakeholder Engagement (CSE) that could provide a basis for such considerations[22].

Given the BSI's experience in the development of consensus standards with the involvement of a broad range of stakeholders, it would be well placed to take a lead in devising a new approach to RRI that provides a more equitable basis for the allocation of responsibility across a range of actors, organisations and sectors. This could involve development of a series of RRI standards tailored to the needs and challenges of specific industry sectors, involving a broader range of stakeholders than is currently the case (beyond those identified simply as 'citizens' or 'members of the public'), including industry, regulators and policy makers. The emphasis could usefully be on

[22] http://www.innogen.ac.uk/downloads/Innogen-Institute-Research-Outline.pdf

balance and proportionality to counter the current excessive reliance on a precautionary approach that encourages social amplification of uncertainty (Nowotny, 2016).

5.4.5 A framework standard for RRI

The term 'aspirational standard', widely used but rarely defined in law, ethics, business and social policy, is often contrasted with 'mandatory standards' which have formal authority. It does not yet seem to have a role in the lexicon of national and international standards bodies, but the BSI has made reference to it in its response to the Lambert Review, noting that "… the process of creating aspirational standards already exists in the form of the national standards making process, for which responsibility lies with BSI as the National Standards Body."[23] This form of standard could be a useful starting point for considering the development of a standard focusing on future developments in RRI.

One potential format could be an umbrella aspirational framework standard that takes account of the various expectations and needs of all stakeholders, and development under that umbrella of specific consensus standards for the needs of different industry sectors and of a broad range of actors, including regulators, policy makers and citizens/stakeholders.

[23] http://www.bsigroup.com/en-GB/about-bsi/media-centre/press-releases/2014/May-2014/BSIs-response-to-the-Lambert-Review-Final-Report-/#.VvlJveIrK1s

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ANNEX 1

Interviewees and areas of expertise

Organisation	*General*	*Autologous cell therapies*	*Industrial Biotechnology / Synthetic Biology*	FinTech
OECD (2 interviews)	✓		✓	
EuropaBio	✓		✓	
Ex-EMA, Regulatory Consultant	✓	✓		
Lawyer	✓	✓		
EU Risk Forum: MNC representative organisation	✓		✓	
International consultancy working in: audit, finance, risk, strategy and technology (3 members of staff)	✓	✓		✓
TOPRA*, large MNC	✓	✓		
TOPRA*, mid-sized MNC	✓	✓		
Academic, regenerative medicines manufacture		✓		
Company, not-for-profit (2 interviews)		✓		
Regulatory affairs consultancy		✓		
Academic lawyer		✓		
Industry support organisation (2 interviews)			✓	
Regulator (Health and Safety)	✓		✓	
Industry support organisation and commercial company (2 interviews)				✓
Industry support organisation				✓
Company, advisor to industry				✓
Financial regulator (2 members of staff)				✓

* Professional membership organisation for individuals working in health regulatory affairs

ANNEX 2

Project Outline

Joyce Tait and Geoffrey Banda

Innogen Institute Background and Experience

The Innogen Institute (Institute for Innovation Generation) has developed an analytical framework that forms the basis for this project (http://www.innogen.ac.uk/downloads/Innogen-Institute-Research-Outline.pdf). It supports company, policy and regulatory decision making in translating research findings to advanced innovative technologies and has been applied across a diverse array of industry sectors.

The Context

This research project, supported by the BSI, will analyse the complementary and potentially competing roles of regulations, standards and regulatory guidelines in unlocking successful innovation, accelerating technology commercialisation and increasing the return on UK investments by making it more attractive to locate and to expand businesses in the UK.

Research outline

We will consult with policy makers, regulators and industry representatives and adapt our framework to enable them to evaluate the individual and joint roles of standards and regulations in unlocking the commercial potential of emerging technology value chains whilst continuing to ensure safety, quality and efficacy. The framework will be capable of adaptation to a range of technologies and applications in different sectors of the economy, the examples adopted in this case being:

(i) personalised medicine manufacture for autologous cell therapies;

(ii) industrial biotechnology/synthetic biology; and

(iii) financial technology (FinTech).

An additional component of the framework will be the extent to which a standards approach could contribute to ensuring Responsible Research and Innovation (RRI).

Based on an analysis of previous research in these areas and our interviews with experts we will endeavour to ensure that our proposed approach is feasible and will potentially support innovation in a manner that is proportionate, effective, safe and affordable.

The outcome

This project started on 1st November, 2015 and the first draft of the report will be completed by 31st December 2015. Further consultation on the draft proposals will be undertaken by BSI in a workshop or series of workshops with interested parties to be held in February 2016, the outcomes of the workshop(s) contributing to the final report, to be delivered in March 2016.

ANNEX 3

Proportionate and Adaptive Governance of Innovative Technologies: the roles of regulations, guidelines and standards

This project[24] is undertaking a scoping analysis of the potential roles of standards in enabling more adaptive approaches to the governance of advanced innovative technologies. The interview will take the form of a structured conversation, covering the questions outlined below in general and, where relevant to your expertise, in the context of three case studies:

(i) personalised medicine manufacture for autologous cell therapies;

(ii) industrial biotechnology/synthetic biology; and

(iii) financial technology (FinTech).

Based on interviews with experts in policy, regulatory and industry communities we will endeavour to ensure that our proposed approach is feasible and will potentially support innovation in a manner that is proportionate, effective, safe and affordable.

Questions to be covered

1. How would you describe the relationships between regulations, guidelines and standards in life sciences and other advanced technology innovation areas?
2. Where and how could standards work more effectively in tandem with regulations or guidelines developed by regulators in support of innovation?
3. Where are there opportunities for national and international standards bodies to work more effectively with national and international regulators on such questions?
4. Where there is a need for a legally enforceable governance system, what needs to be done to ensure that a standard or regulatory guideline is auditable and who should do the auditing?
5. We are presuming several advantages of standards over regulations - faster to develop, done in collaboration with innovators, easier to change/adapt, more supportive of innovation –are these valid assumptions?
6. Regarding the distinction between radical and incremental innovation – are the roles of standards and regulations different in each case?
7. In the early stages of development of an advanced innovative technology there will be a stage where a decision on the appropriate form of the regulatory system has yet to be taken. What role could standards play in regulatory decision making in these early stages of governance of an innovative technology?
8. Scientists and innovators are increasingly being required to demonstrate that they are incorporating a consideration of Responsible Research and Innovation (RRI) within their routine practices. Is there a role for standards in codifying these requirements in a way that is compatible with the needs of innovators? If so, how would you like to see this role formalised?

[24] Project undertaken by the Innogen Institute, University of Edinburgh, funded by the British Standards Institute