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Developing standards to support the synthetic biology value chain

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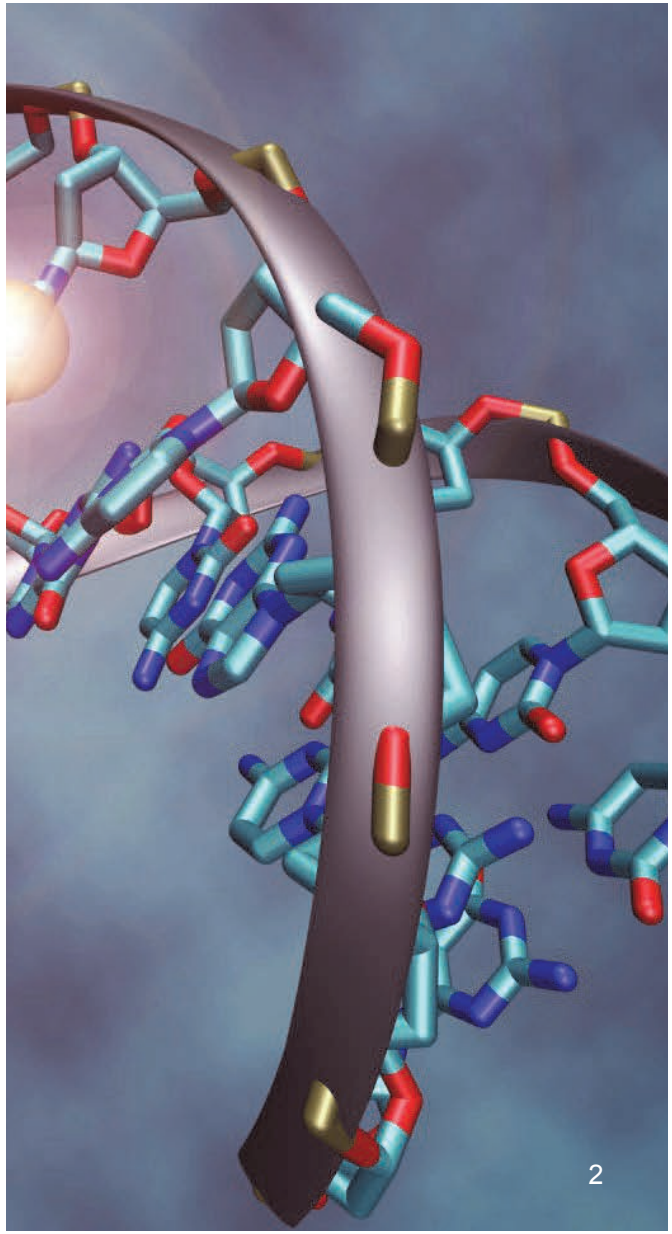

Preface

This report, commissioned by the British Standards Institute, provides an analysis of the value chain in synthetic biology and the barriers, challenges and opportunities inherent within it. By conducting a rapid review of the literature and speaking with over 30 companies, end-users and public sector stakeholders, we identified a series of findings and recommendations about the nature of the value chain, the barriers and challenges within it, and the role standards could play in the future. The report will be of interest to the wider synthetic biology community, as well as researchers, policymakers, and industrial players.

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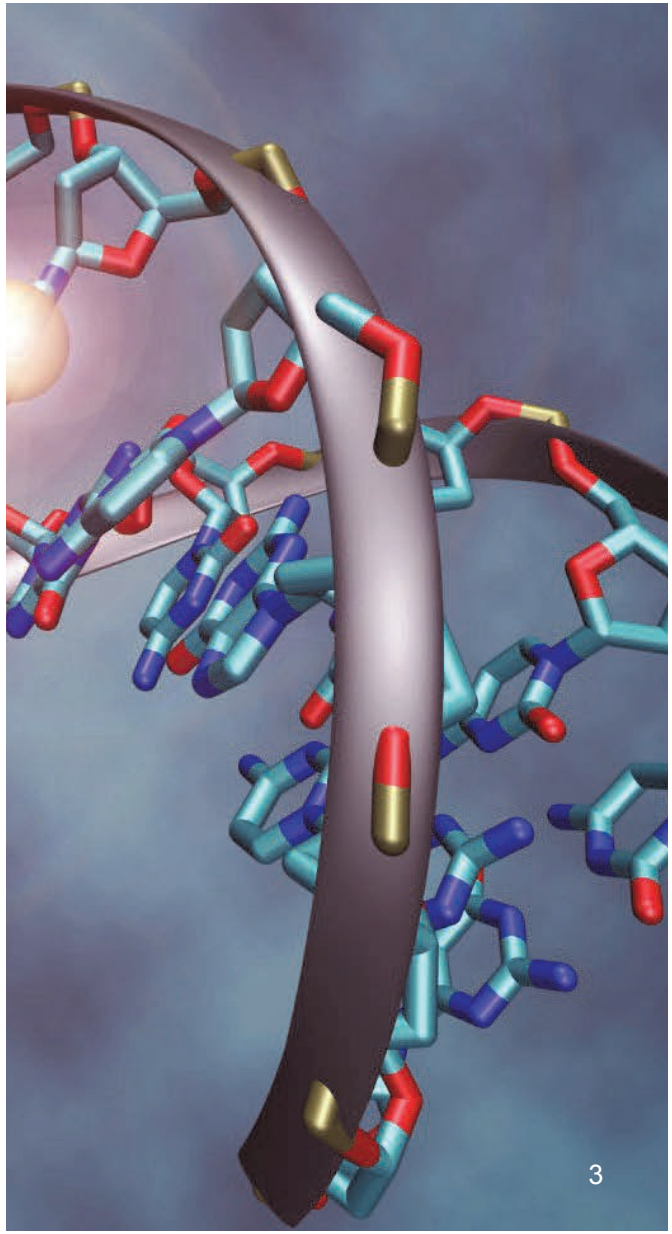

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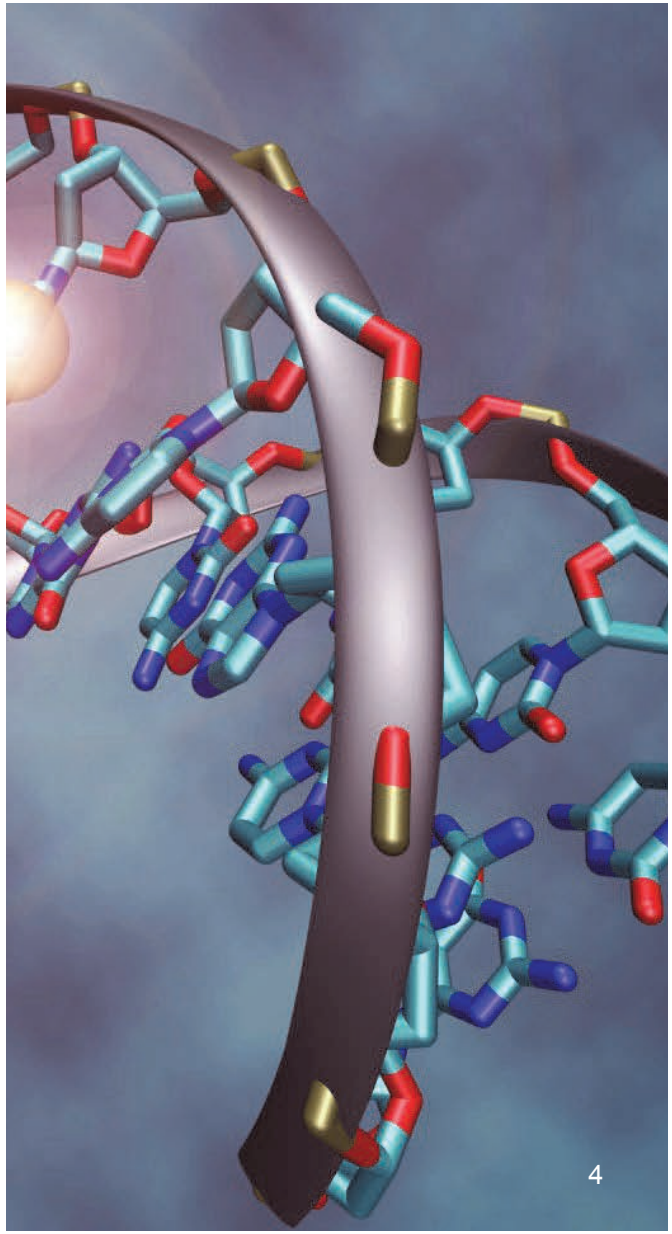
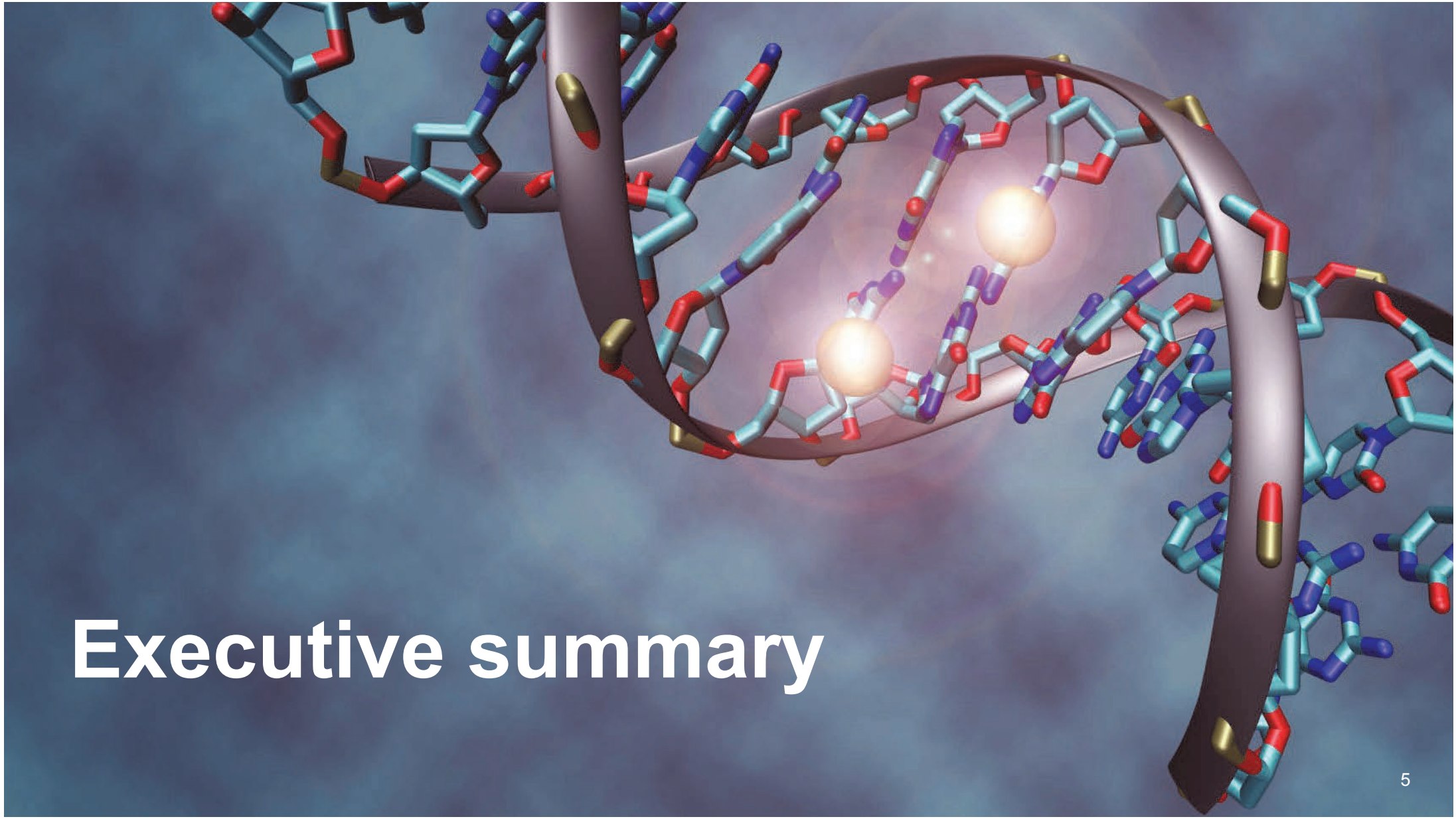




Executive summary

Executive summary

- **The overarching aim of this study was to identify the impact that adoption of synthetic biology is likely to have on the global marketplace** (buyers, sellers and users) as well as any existing barriers or obstacles preventing the rapid scale up and commercialisation of the technology.
- **Synthetic biology can generally be thought of as a platform technology that enables the design and engineering of biologically based systems.** As a field of science it encompasses both the biological aspect of designing systems to help understand them, and the engineering aspect of designing systems with the aim of achieving a set endpoint. Thus, it involves the design of new living systems that can carry out specific functions or produce products.
- **Most of what is being commercialised now is a new process for producing a product, and it will likely be five to fifteen years before many entirely new synthetically modified products are on the market**. Current synthetic biology products range from organisms developed to produce flavours and fragrances identical to those derived from a plant, to mosquitoes designed to breed infertile offspring that may be used to control the Zika epidemic.
- **In the study, we used the concept of a value chain to aid our analysis of the synthetic biology sector**. We have made a novel contribution to the field by developing the following characterisation of the value chain:
    - It starts with an **idea** of the product to be produced, and then the engineering steps of **design, build, test** repeated until the desired product is produced. Each of these steps draws on various computational or physical inputs that may come from other companies in the value chain as an additional service or product. There is then a final **scale-up** process to produce enough product for it to be usable as a product in its own right, or within other industries.
- **The synthetic biology value chain interacts with the value chains in other sectors in two main ways:**
  i) *absorption*, where parts or all of the value chain of synthetic biology are used themselves within a sector-specific company; ii) *selling in*, where a product is designed through synthetic biology in a company and sold into the production step of a specific sector. Both of these *upgrade* the other sector's value chain through the inclusion of synthetic biology.

Executive summary

- **Through the interviews and literature review, we identified a series of drivers and factors that will influence the field of synthetic biology in the future** and classified them according to a PESTLE framework (Political, Economic, Social, Technological, Legal or Environmental):
    - The main *political factors* are driven by uncertainty over future regulation and the lack of coordinated international efforts.
    - There are more *economic* factors affecting synthetic biology than any other driver. It is considered a risky and expensive business by investors and there is a negative feedback loop that is difficult to break.
    - The *social* factors likely to have an impact on the development of synthetic biology are associated with the social acceptability of synthetic biology products. The social acceptability is linked to the anticipated balance between benefits and perceived risks by the general public.
    - *Technological* factors include the poor reproducibility of engineered organisms and poor interoperability of R&D protocols. This results in slow engineering processes and a perceived lack of scientific advancements.
    - Synthetic biology companies and regulatory authorities view the nature of *legal* factors differently.
    - The main *environmental* factors likely to have an impact on the development of synthetic biology are associated with the potential threat of released synthetic biology organisms on biodiversity and on human health.
- **We found a range of barriers and challenges to commercialisation that were expressed by the companies we interviewed.** These were mapped along the stages of the value chain to reflect differences between companies:
    - **There were three main challenges identified at the *idea* stage**: i) the current level of scientific knowledge makes it hard to make the most of what synthetic biology promises; ii) there is a reluctance/inertia of established companies to change and adopt synthetic biology; iii) there is a lack of communication and understanding between industry and academia and a poor exchange of information between different companies.
    - **At the *design-build-test* stage the following barriers were thought to exist**: i) the current level of scientific knowledge; ii) poor exchange of information; iii) lack of integration and innovation around equipment; iv) intellectual property rights.
    - **The most numerous barriers and challenges emerged at the *scale-up* stage**: i) reluctance/inertia of companies to change; ii) difficulties in maintaining a revenue stream; iii) lack of a notable financial success; iv) regulatory hurdles; v) the level of scale up required to have a good return on investment; vi) negative public perception; vii) concerns about environmental release; and viii) intellectual property rights.

Executive summary

- **Alongside the barriers and challenges, companies and stakeholders identified the different benefits of standards for various stages of the value chain:**
    - At the ***idea stage***, standards could help establish synthetic biology as a fully defined field of research and commercial opportunity. Standards could also improve communication within the research and industrial community and help to bridge different sectors by providing a common vocabulary. Technical standards could resolve some of the problems that currently take up resources by providing specifications for input and output values.
    - At the ***design-build-test stage*** standards could: i) help with the interoperability of the equipment and improve the workflow with providers and buyers and ii) enable innovation by facilitating competition between and within technologies. Open standards were thought to be important for facilitating superior IP for end-products.
    - At the ***scale-up stage***, standards could improve the efficiency of regulatory processes; allow for reproducibility and reduced transaction costs, therefore allowing greater productivity; enable the emergence of innovative products; increase trust; address environmental containment concerns.
- **The interviewees also highlighted several challenges and concerns with standard setting.** While the overall opinion on standards was positive, they cannot be considered the solution to every problem in synthetic biology, and there will be instances where they could block innovation or render the activities of some companies obsolete.
- In order to help us explore how standards might affect the value chain in the future, we developed four different scenarios. These were used to explore future opportunities for synthetic biology and to test the role standards might play. The four scenarios were:
    - *Catastrophe leads to containment*, which is a future characterised by a very conservative regulatory environment.
    - *Synthetic biology for the public good*, which envisages that the synthetic biology value chain is driven by a need to develop goods and services that serve the public good.
    - *Synthetic biology and the 'entrepreneurial state'* is a scenario that proposed a synthetic biology value chain driven by high financial investment from the state.
    - *The sharing economy model* scenario proposed a space dominated by many specialised smaller companies.
- **The scenario analysis brings out several features that standards and regulations can play on the nature of innovation in synthetic biology and the configuration of the value chain.**

Executive summary

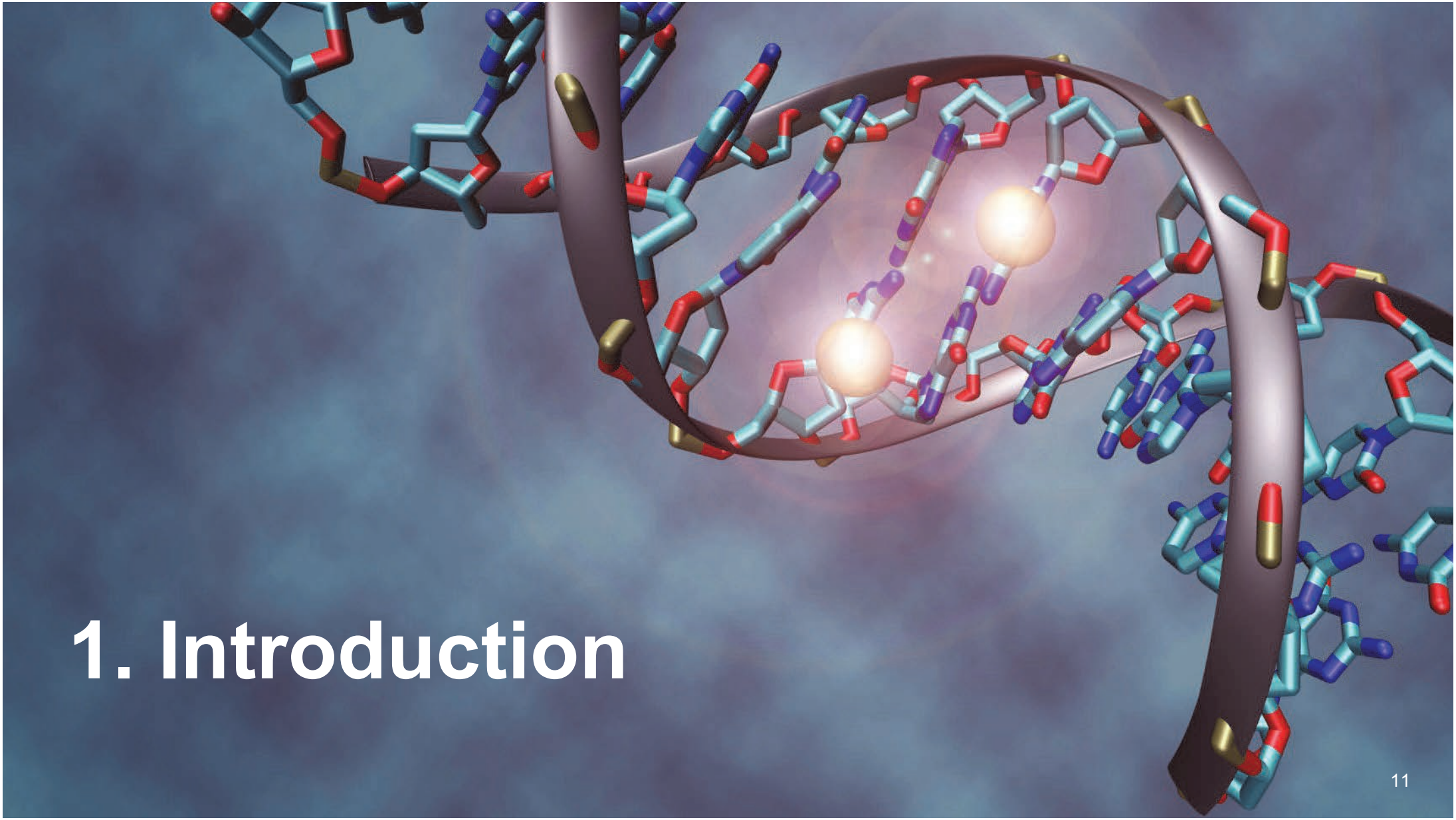
In conclusion, this report contains an array of issues relating to the nature of the synthetic biology value chain, the future evolution of the synthetic biology sector and the barriers, challenges and opportunities facing it. Standards can and should play an important role in this future. However, there will inevitably need to be a period of reflection and consideration on the ways to act. On this basis, the following findings and recommendations are put forward:

- **Companies we interviewed do think that standards will help reduce uncertainty and help to overcome a variety of barriers they encounter en route to commercialisation.** BSI and other stakeholders should take the opportunity to build on the findings in this study and catalyse efforts to advance standard development for the field in a variety of areas.
- **Together with stakeholders, BSI should prioritise the stages of the value chain presented in this report for future standard development.** Although it is a long way off for some companies, most challenges were perceived at the scaling-up stage and it could be that a focus on this stage now could have knock-on effects upstream in the value chain.
- **In setting standards, do not lose sight of the importance of 'soft' standards, which can facilitate norms and behaviours within the sector, as well as affect how synthetic biology is perceived by society.**
- **Monitor the nature of innovation that is desired within value chains and be conscious of how standards may affect both incremental and disruptive innovation.**
- **Use standards to address public trust and confidence in the future market, as well as to identify key benefits for end users, including the general public.**
- **Standards could contribute to synthetic biology being perceived not only as an interesting domain of research, but one that is becoming more defined as a sector in its own right (with its own value chain(s)).**
- **We found only a few differences between US and UK companies. These were primarily related to the different market opportunities and investment climates in each country.** While the US seems to have a more conducive climate for private investment, it was felt synthetic biology enjoyed more government support in the UK. Both sets of conditions will be important in different ways for synthetic biology and standards can help facilitate private investment, as well as complement and work alongside government priorities.

Executive summary

The final set of points below raise a series of issues, in the form of provocations and questions for the future, which are worth considering on the basis of our analysis.

- **The analysis of the value chain presented here is novel and could be used to frame discussions for the sector.** It will be interesting and important to consider the framework for the different stages of the value chain presented here and the ways in which synthetic biology feeds into other sectors – particularly through absorption and selling-in. Monitoring this as the sector grows will be an important area of ongoing research that could help to structure priorities for future standard development.
- **What should the role of public–private partnerships be and how can they help to overcome market and institutional failure?** Standards could play a role in identifying and supporting areas for public–private partnerships to maximise the potential of synthetic biology and overcome market and institutional failures. However, this will need to be monitored closely as sectors bring the benefits of synthetic biology closer to the market.
- **What future scenario would BSI and its stakeholders like to see realised and what elements from the four scenarios here could help that?** Is a diverse value chain with many small companies desirable? Is a highly entrepreneurial state needed now, but with a view to helping move towards a more market-driven scenario in future? Working with stakeholders to determine elements of future scenarios that are desirable will be important to understanding and determining shaping actions that can be taken today.
- **Due to the enabling role synthetic biology can play, there may be a need to look at how standards intersect with other industrial ecosystems, in particular in light of the global nature of the sectors it will play a role in.** As synthetic biology often enables other industries, it is possible that in some industries the development of standards that could push this field forward might be countered by some players due to market forces. The success of standards should be judged taking into account the ecosystem of each industry.



1. Introduction

Introduction

Outline of section

This section provides the background context and methodology for the study. We describe what is meant by the term synthetic biology, give a short overview of initiatives and actors in synthetic biology in the UK and introduce the concept of standards as a governance tool to support innovation.

Core messages

- The overarching aim of this study is to identify the impact that adoption of synthetic biology is likely to have on the global marketplace (buyers, sellers and users) as well as any existing barriers or obstacles preventing the rapid scale up and commercialisation of the technology.
- Synthetic biology can generally be thought of as a platform technology that enables the design and engineering of biologically based systems. As a field of science it encompasses both the biological aspect of designing systems to help understand them, and the engineering aspect of designing systems with the aim of achieving a set endpoint. Thus, overall it involves the design of new living systems that can carry out specific functions or produce products.
- Current synthetic biology products range from organisms developed to produce flavours and fragrances identical to those derived from a plant, to mosquitoes designed to breed infertile offspring that may be used to control the Zika epidemic.
- Most of what is being commercialised now is a new process for producing a product, and it will likely be five to fifteen years before many entirely new synthetically modified products are on the market.
- There are currently a variety of initiatives and actors supporting synthetic biology in the UK and globally.

Why this study?

The overarching aim of this study is to identify the impact that adoption of synthetic biology is likely to have on the global marketplace (buyers, sellers and users) as well as any existing barriers or obstacles preventing the rapid scale up and commercialisation of the technology. Though much work has been done looking at the research, political, social and technological challenges, very little of this has focused on the issues from the perspective of the companies themselves. Current challenges that need to be addressed in this light include:

- Identifying the ways in which companies are currently interpreting the potential of synthetic biology and to map the contours of the commercial development landscape as it is now and as it might evolve.
- Identifying the enablers and constraints in the current commercial and innovation environments.
- Involving public and private stakeholders in dialogue about ways in which to facilitate shared synthetic biology growth agendas.

Building on this, this study aimed to:

- Map the UK and US synthetic biology value chain(s), including identifying companies with products and services close to market, and describe how it might evolve in the future.
- Identify barriers and challenges facing synthetic biology companies and explain how those barriers may differ depending on the companies' position in the value chain.
- Identify barriers and challenges preventing potential end-users (e.g. large pharmaceuticals or consumer goods manufacturers) from adopting synthetic biology.
- Identify and test the viability of different types of standards that would help companies and end-users overcome some of the barriers and challenges identified.
- Produce recommendations for standardisation activities likely to yield the most value for the synthetic biology industry and potential adopters of this technology.

Methodology

There were five main tasks for this study. In Task 1, **collating existing knowledge**, we discussed the project aims and objectives with the client and our senior advisors in order to collate existing knowledge of companies and the value chain. Tasks 2 and 3 then proceeded in parallel.

In Task 2, **the rapid evidence review**, we i) mapped and refined the synthetic biology value chain and developed appropriate categorisation schema for companies and services within it and ii) identified an initial set of barriers and challenges that would be tested and further explored in the interviews. In Task 3, **the key informant interviews**, we held 33 interviews with 26 stakeholders (26 individuals were interviewed, and 7 of these were interviewed again for Task 4). This enabled us to explore in more depth the issues relevant to the value chain, including categorisation of private sector companies and actors, and the barriers and challenges faced. The semi-structured interviews lasted up to one hour and included the following types of stakeholders: representatives of private sector companies (both SMEs and large multinationals, and from across different sectors and stages of the value chain), representatives from US and UK public bodies, and representatives from academic initiatives in synthetic biology. It is worth noting that it was most difficult to identify and recruit end-users for our study (we will come back to this point later in the study). A description of stakeholders interviewed is included in Annex 1, an interview protocol in Annex 2, and a set of search terms and sources reviewed for the rapid evidence review is in Annex 3.

In Task 4, **analysis of scenarios and testing of future scenarios**, we drew together the evidence base in a way that allows us to understand how standards could address barriers and opportunities and the implications of this for the value chain. These scenarios were developed in an internal workshop and then tested with a subset (n=7) of the stakeholders from Task 3.

Finally, in Task 5, **reporting**, we summarised key findings and recommendations, drawing together all the evidence from across previous streams.

The findings presented in this report are based on evidence collected through the first three tasks and, notably, are heavily based on actual company perceptions of barriers, challenges and opportunities in the field of synthetic biology and the role standards might play in future. All findings are supported by views expressed by at least several interviewees, and in many cases on a majority of views. The cross-cutting analysis in the final sections is based on our synthesis of all of this evidence. All quotes used in the report are illustrative of particular points made in the analysis.

Caveats and limitations

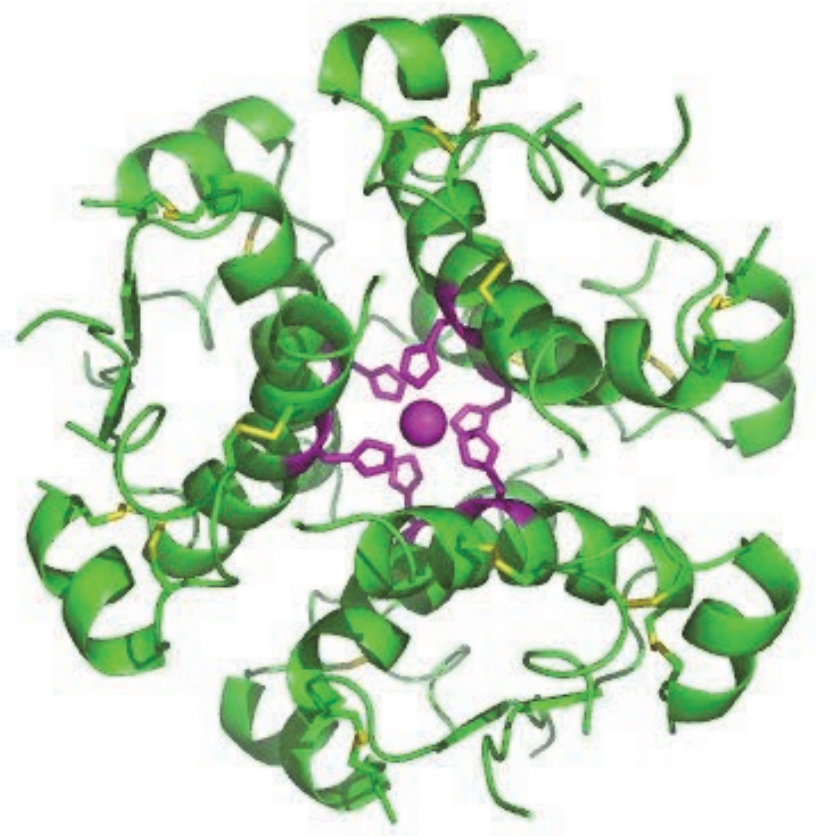
There are a series of caveats and limitations to this study that should be pointed out before proceeding.

- We initially compiled a list of over 200 companies active in the synthetic biology sector in the UK, US and Europe. The time and resources available for this project meant we were only able to speak to 26 stakeholders. However, we did find that as the interviews progressed similar issues began to emerge, which is often a sign in qualitative research that your main research questions have been addressed.
- Our analysis was limited by the extent to which we were able to receive a similar nature of responses from all interviewees. Our interview protocol was semi-structured, and so some interviewees spent more time on some questions than on others. They also highlighted barriers and challenges that were most relevant to their position in the value chain, rather than being asked to comment on a long list of barriers and challenges we had identified in advance. This meant that we were limited in the extent to which conclusions could be drawn which highlight a majority view across all interviewees, or indeed the extent evidence could even be quantified. Indeed, we were most interested in drawing out the diversity of perspectives across the interviews as this lends itself to a richer and more nuanced analysis.
- Our ability to recommend specific types of standards was limited by the feedback from companies. They recommended broad areas for standard development, which we report on here.
- This study was not intended to explore in detail issues related to intellectual property, regulations or other governance instruments for the sector and so we do not go into great detail on these points.
- As the scenario analysis was not a core feature of our overall study, we were limited in the extent to which we could explore the effect of all drivers on the different outcome axes. We suggest that in the future this exercise could be conducted by BSI or other interested stakeholders in the ways suggested in the slides.

What is synthetic biology?

Synthetic biology can generally be thought of as a platform technology (a technology from which other things can be developed), which enables the design and engineering of biologically based systems. As a field of science it encompasses both the biological aspect of designing systems to help understand them, and the engineering aspect of designing systems with the aim of achieving a set endpoint. Thus, it involves the design of new living systems that can carry out specific functions or produce products. It treats segments of DNA as parts that can be copied, cut and moved around to build these new systems. Key developments in synthetic biology were carried out in bacteria and yeast and many emerging applications of synthetic biology also focus on the use of these organisms [1].

However, ‘synthetic biology’, itself, is not necessarily a well-defined term. This is in part due to its broad range of applications, but also because it is an emerging technology that continues to evolve. While interviewees varied on their exact definition, they tended to agree that synthetic biology is not in itself a radically new field, but is rather an evolution of molecular biology and genetic engineering that has been enabled by both scientific and technological advances. The most common description given was that it is genetic engineering with real engineering principles incorporated in it. A key engineering principle that was mentioned frequently is that of iterative design, where there is a design-build-test cycle, where in each cycle learning takes place and the product is refined and improved.



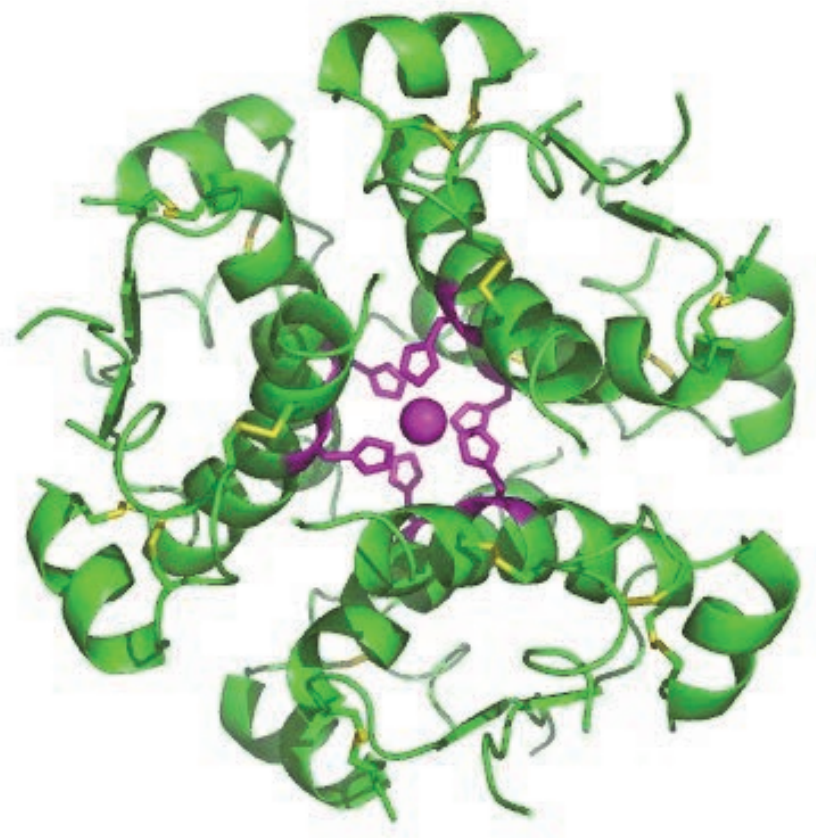
What is synthetic biology?

The engineering aspects of synthetic biology lend it to a wide range of opportunities for commercialisation. Current products range from organisms developed to produce flavours and fragrances identical to those derived from a plant, to mosquitoes designed to breed infertile offspring that may be used to control the Zika epidemic. Interviewees mentioned a variety of possible future applications, including: environmental clean up, new drugs (including antibiotics), organisms able to diagnose and treat illnesses, new vaccines, microbial control, producing plastic from waste gases, agriculture products addressing some social issues (e.g. food security), new products in the field of personalised medicine or gene therapy, and also new fuels and chemicals that could help to mitigate the effects of fossil fuels.

Synthetic biology products can generally be classified into two types.

- Those where the process for producing the product uses synthetic biology, but the product itself is not alive and is the same, or very similar to the current product.
- And those where the product itself has been modified synthetically.

While both of these types of product are likely to get more numerous in the coming years, interviewees noted that most of what is being commercialised now is a new process for producing a product, and it will likely be five to fifteen years before many entirely new synthetically modified products are on the market.



There are a variety of initiatives and actors supporting synthetic biology in the UK and abroad

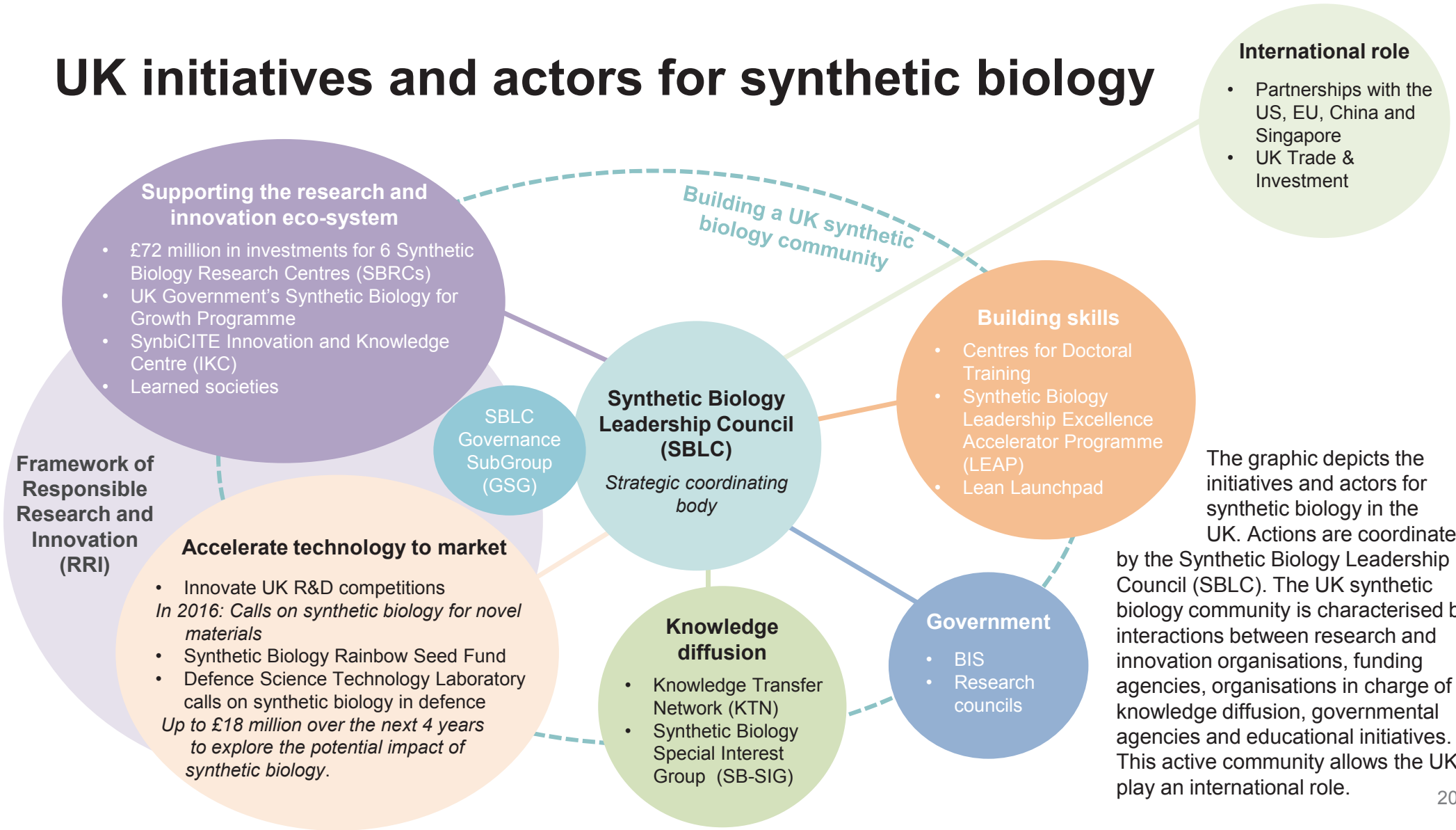
- Synthetic biology has been identified as one of the ‘eight great technologies of the future’ by the UK government. It benefits from strong investments from the UK government [1], amounting to approximately £300m in the last 8 years [2]. The UK’s synthetic biology roadmap in 2012 aimed to ‘help companies develop new products, processes and services of clear public benefit, generate economic growth and create jobs’ [2] (see Table 1) .
- In February 2016, the Synthetic Biology Leadership Council published a new UK Synthetic Biology Strategic Plan 2016 with a stronger focus on the translation of emerging ideas, the commercialisation of applications, and deployment to global markets. It aims to establish a £10bn synthetic biology based platform technology industry by 2030.
- In the EU, the EraSynbio project funded by the European Commission has a strategic plan to encourage the development of a coherent and coordinated European policy framework. This has triggered initiatives to foster European cooperation [3].
- At the international level, the US has a considerable industry that benefits from strong government support [4]. Other countries such as China have identified synthetic biology as a key priority area [5]. There are also international cooperation programmes such as the Six Academies series (UK-US-China), the UK-US joint research calls for synthetic biology, the EU-US Task Force on Biotechnology Research, and the EraSynbio Joint calls to fund EU-US scientific collaborations [6]

There are a variety of initiatives and actors supporting synthetic biology

Table 1. 2012 UK Government's Roadmap recommendations and progress made

1. Invest in a network of multidisciplinary centres to establish outstanding UK synthetic biology resource	Six multidisciplinary research centres in synthetic biology have been established supported by a £72m investment from the UK government.
2. Build a skilled, energised and well-funded UK-wide synthetic biology community	The synthetic biology community is comprised of funding agencies, UK government, research and knowledge diffusion organisations, and education institutions and is becoming increasingly networked, leading to cross-disciplinary interactions. The Synthetic Biology Special Interest Group (SB-SIG) facilitates those interactions.
3. Invest to accelerate technology responsibly to market	A Framework of Responsible Research and Innovation (RRI) has been developed to strengthen social awareness and public acceptability. Innovate UK and Defence Science and Technology Laboratory competitions aim to support the commercialisation of research outputs.
4. Assume a leading international role	The SBLC expects that the development of a strong synthetic biology community will give the UK an international reputation and position the country as an international leader. Partnerships have already been established between the EU, US, China and Singapore.
5. Establish a leadership council	The Synthetic Biology Leadership Council has been established to 'strategically oversee the development of a successful SynBio industry sector in the UK'. The SBLC has formed a Governance Subgroup, which provides support and advice to the SBLC and encourages an open, adaptive and consultative approach to governance within the synthetic biology eco-system.

UK initiatives and actors for synthetic biology



The graphic depicts the initiatives and actors for synthetic biology in the UK. Actions are coordinated by the Synthetic Biology Leadership Council (SBLC). The UK synthetic biology community is characterised by interactions between research and innovation organisations, funding agencies, organisations in charge of knowledge diffusion, governmental agencies and educational initiatives. This active community allows the UK to play an international role.

The role of standards in innovation

A standard is a tool that aims to set out *clear and unambiguous provisions and objectives*, so that they can help *facilitate common working practices/relationships across a sector*. Standards differ from other types of rules that govern innovation. Regulations, guidelines and standards can all be seen as different types of *innovation governance instruments.* While they all involve a set of rules, they have several distinguishing features.

- Regulations and guidelines are based on legislation and are usually developed by regulatory bodies. Adoption of regulations is mandatory with punitive actions from the state in case of transgression. Guidelines are seen as soft law instruments that support regulations.
- Standards usually have a voluntary nature and are based on recommendations and consensus among all parties involved. They bear the stamp of approval of a recognised standardisation body rather than a regulatory authority. A de facto standard is adopted by the public, while a de jure standard is endorsed by formal standards organisations.

There are many ways of categorising standards [1]. A basic typology is:

- **Technical**, providing specifications for how something is made (e.g. input and output values such as materials that are used as calibrators in assays).
- **Procedural**, describing workflows (e.g. standard operating procedures such as ICS 25.020 Manufacturing forming processes, Good Manufacturing Practice, ISO 9000 quality management system).
- **Classifying**, providing definitions towards a common vocabulary (e.g. Braille, International maritime signal flags, International Code of Signals).

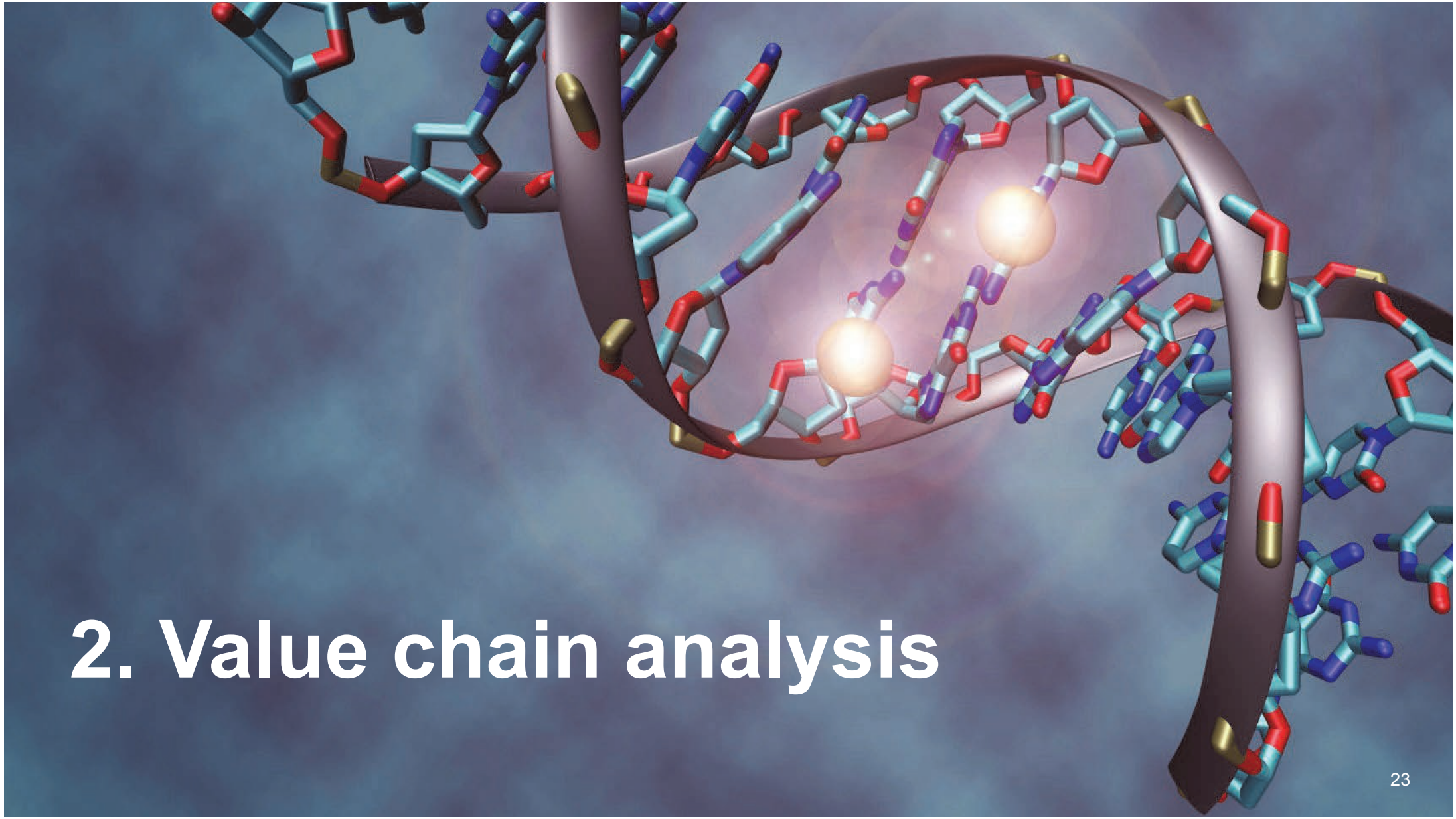
> **Regulations, guidelines and standards can all be seen as different types of *innovation governance instruments***

The role of standards in innovation

Standards can also have a temporal or market-based context. They can be introduced in anticipation of new innovations, as a way to encourage participation in emerging technologies, or can be responsive to new innovations. The timing of when a standard is set is important as it impacts economic efficiency. A premature standard could lock an industry into a technology, possibly affecting the adoption of other cost-saving technologies, whereas a delayed standard could be ignored, even if it could bring about economic benefits [1]. In a complementary way, standards can help to support production or technology development. By thinking of the product life-cycle and the maturity of the market, stakeholders can consider the priority areas for standards to be developed in [2].

A number of endeavours for developing standards in synthetic biology exist. To date, most of these efforts have been led by the research community. The discussions are concentrated on developing standards for measurement, characterisation of parts, and data exchange. Information on ‘softer’ standards that could address the societal concerns and wider industry issues, such as codes of ethics or ways of dealing with intellectual property rights, are a feature, but there has been little consensus.

A number of endeavours for developing standards in synthetic biology exist



2. Value chain analysis

Value chain analysis

Outline of section

A core element of our analysis was identifying and articulating the nature of a value chain in synthetic biology. In this section we discuss what a value chain is, how they can be used as an analytical tool, and present one possible configuration of the synthetic biology value chain based on the information provided to us during the interviews and our own analysis for this study.

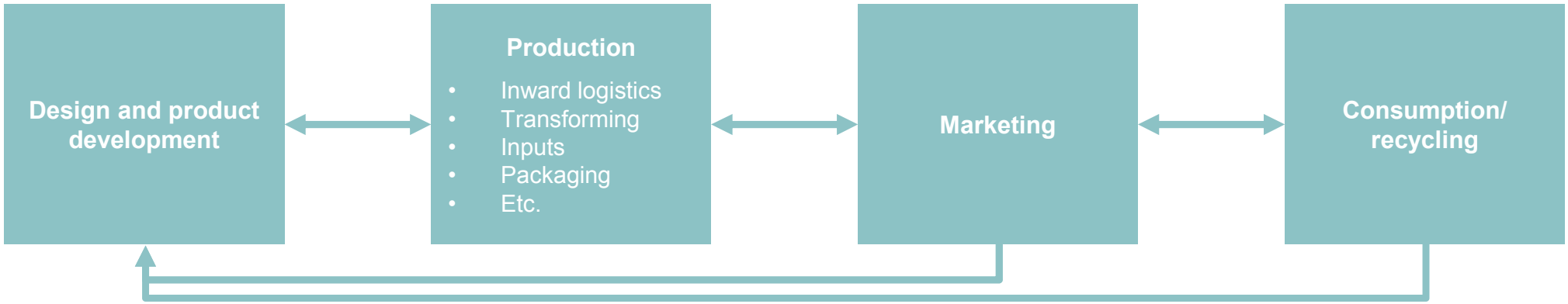
Core messages

- Value chains are a helpful tool for describing and subsequently analysing the 'full range of activities that firms and workers do to bring a product from its conception to its end use and beyond' [1].
- The synthetic biology value chain starts with an **idea** of the product to be produced, and then the engineering steps of **design, build, test** repeated until the desired product is produced. Each of these steps draws on various computational or physical inputs that may come from other companies in the value chain as an additional service or product. There is then a final **scale-up** process to produce enough product for it to be usable as a product in its own right, or within other industries.
- The synthetic biology value chain interacts with the value chains in other sectors through: (1) **absorption**, where parts or all of the value chain of synthetic biology are used themselves within a sector specific company and (2) **selling in**, where a product is designed through synthetic biology in a company and sold into the production step of a specific sector. Both of these **upgrade** the other sector's value chain through the inclusion of synthetic biology.
- Synthetic biology has possible applications in a wide variety of sectors. Currently it is most used in the pharmaceutical and fragrance and flavours sectors.

What is a value chain?

Value chains are a helpful tool for describing and subsequently analysing the ‘full range of activities that firms and workers do to bring a product from its conception to its end use and beyond’ [1].

A value chain is made up of value adding ‘links’ between different stages of production. Each link includes a variety of activities that go well beyond simple production, such as the development and design of a product or process, activities related to marketing, and the consumption, as well as recycling of product materials [2].



Value chains, however, rarely capture the full complexity of feedback loops, and interactions. For example, the marketing of a final product may influence the design, hence there would be a feedback loop between the two stages. Additional complexity can occur where one firm provides input into multiple links along a value chain. For example, a chemical manufacturer may provide different types of inputs into the production of a product, or may feed into several different value chains. It is unusual for a value chain to capture the full complexity of activities, but rather it focuses on those key value-adding elements [3].

Value chains help us to understand the role of different firms within a technology area

Activities in a value chain have a flow – so the value chain captures the input and the related outputs at each link. Often a value chain consists of several firms, contributing to activities at different links or providing specific inputs in terms of work, skills, knowledge or other materials that, when combined, add value to the product or service. Alternatively a value chain may be extensively vertically integrated, such that one firm is responsible for the full value chain [1].

Value chains should be distinguished from businesses models [2]. A business model can be regarded as a generic model that describes the processes used to generate value by a particular business (or businesses). Business models are found to reside within particular firms, but do not operate in isolation. A change in one firm's business model can affect the performance of another firm's business model. It follows, then, that the strategy of firms within a particular value chain can have implications for how business models are developed and applied [3].

In the process of identifying how best to apply a particular technology, firms will experiment with different business models to 'capture' different sections of the value chain of a product or service. It may be the case that a value chain including a significant number of activities related to an emerging technology will feature firms with different and competing business models.

Value chains for *emerging* technologies (like synthetic biology) are going to evolve over time

Emerging technologies have been defined as those '…that could exert much enhanced economic influence in the coming (roughly) 15-year horizon.' [1] and are '…in an early phase of development. This implies that several aspects, such as the characteristics of the technology and its context of use or the configuration of the actor network and their related roles are still uncertain and non-specific' [2].

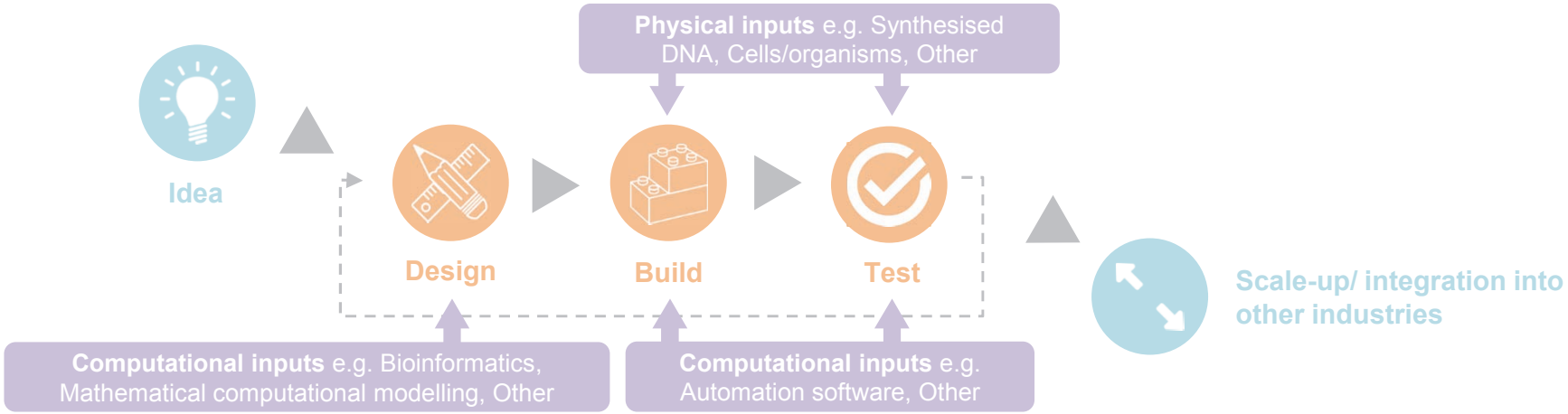
Rotolo et al. (2015) identify five prominent features of most emerging technologies including:

- **Radical novelty** – introduces a significantly different from existing way of doing things. It can be revolutionary in application or process, as well as examples where existing technologies find radically different areas of application from their original use.
- **Relatively fast growth** – where growth can refer to a range of factors including the number of scientists working in the field, number of publications, as well as the growth of firms involved.
- **Coherence** – so that it is possible to identify a community of experts, or group of actors involved in the technology, separate from the original 'parent' firm, or inventors.
- **Prominent impact** – such that the benefits of the technology and impact are pervasive economically and socially and cut across different sectors of the economy.
- **Uncertainty and ambiguity** – the technology is 'unfinished' and still under considerable development, such that future expected outcomes or innovation related to the technology are uncertain and characterised by risk.

Some argue that the key to innovative success is to minimise disruption on the value chain. This is because innovations may have a competency destroying attribute that could have detrimental effects on a new product or process. Related, there can also be appropriability issues, where actors are not able to appropriate the benefits due to high organisational uncertainties. This arises when, even if a new product or process is technologically and commercially viable, there is no guarantee that the innovator will be able to use (appropriate) the innovation.

Overall, what is important to bear in mind is that a value chain involving activities based on emerging technologies are likely to evolve over time as that technology matures. In turn, business models related to a particular value chain will *adapt* and this may have implications for the type and number of firms involved in different value chain activities. For example, a firm with a new technology may be able to apply an innovation to *upgrade* specific activities in an existing value chain. Or, alternatively, the technology may result in fundamentally *new products or services*, thereby creating a new value chain.

One way to organise the synthetic biology value chain is around the ‘design-build-test’ concept

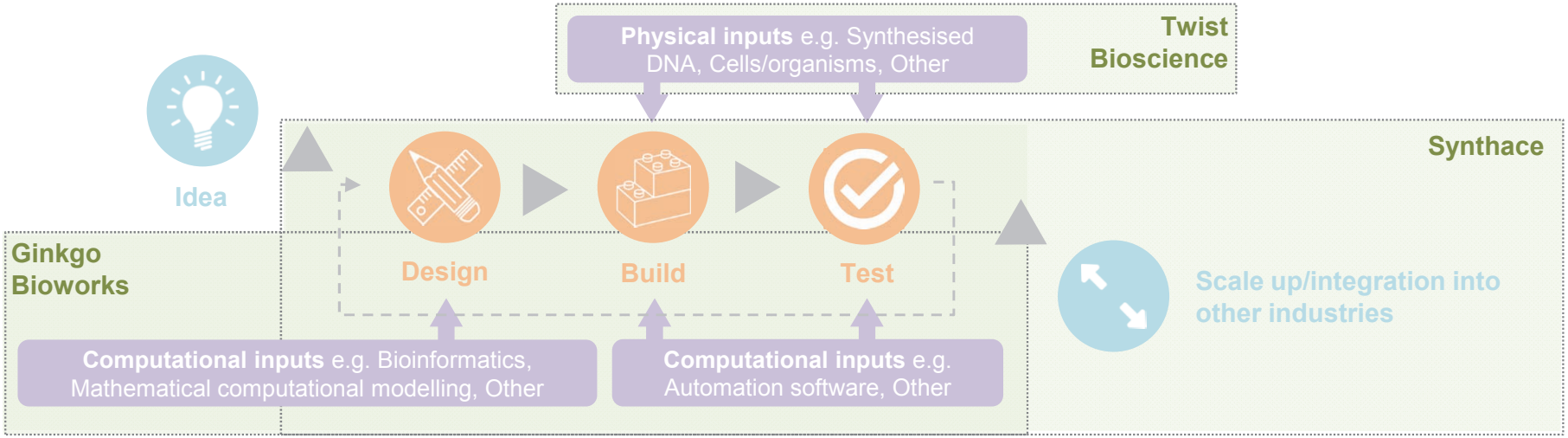


Based on our interviews and subsequent analysis, we propose that the current synthetic biology ‘value chain’, as comprising different products and processes that could be commercialised, centres around the idea of designing organisms to do a certain thing; either to produce a product, or to be the product themselves. While each product will have its own value chain, the links and stages in the value chain are similar across products.

The value chain starts with an idea of the product to be produced, and then the engineering steps of **design-build-test** repeated until the desired product is produced. Each time a cycle is completed, learning occurs and is fed back into the design process. Each step requires different inputs:

- The **design** process is largely computational and its inputs can both be imbedded within some synthetic biology companies, or sold by other companies as a service.
- The **build** and **test** steps have both computational and physical inputs, which again can come from within companies or be sold by other companies, either as a service or as a product.
- Once the desired product has been developed this goes into a **scale-up process** to allow enough of the product to be produced for it to be usable as a product in its own right, or within other industries.

Companies can be mapped onto the value chain depending on their focus…

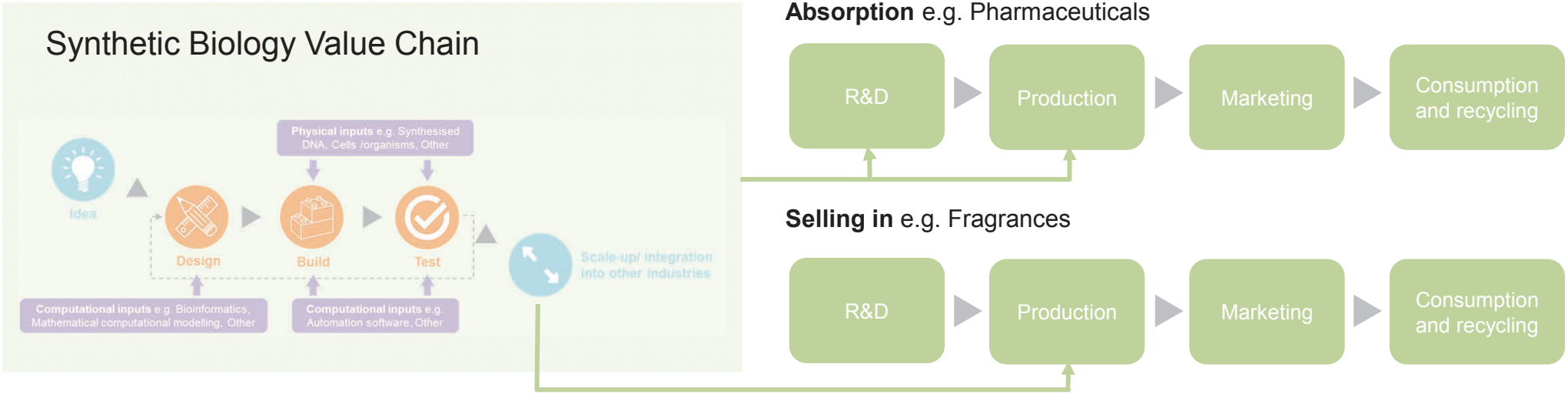


Specific companies, with their own business models, can be mapped onto this chain. For example,

- **Ginkgo Bioworks** is a company specialising in organism design for a variety of sectors, currently focusing on fragrances.
- **Twist Bioscience** is a company specialising in DNA synthesis. They sell synthesised DNA to companies performing synthetic biology, as well as to academic researchers.
- **Synthace** is a technology company that has developed a programming language for codifying biological unit operations. They both create software tools and develop high yielding bioprocesses. As well as organism design they have a focus on the scale-up process.

Please see Annex 4 for other examples of companies we interviewed for this study mapped onto the value chain.

…and further mapped to show the relationship with other sectors – either through absorption or ‘selling in’



As synthetic biology spans a number of sectors, its value chain interacts with the value chains in other sectors. From our interviews we observed two types of interaction:

- **Absorption**, where parts or all of the value chain of synthetic biology are used themselves within a sector specific company. Some pharmaceutical companies are currently using this model.
- **Selling in**, where a product is designed through synthetic biology in a company and sold into the production step of a specific sector.

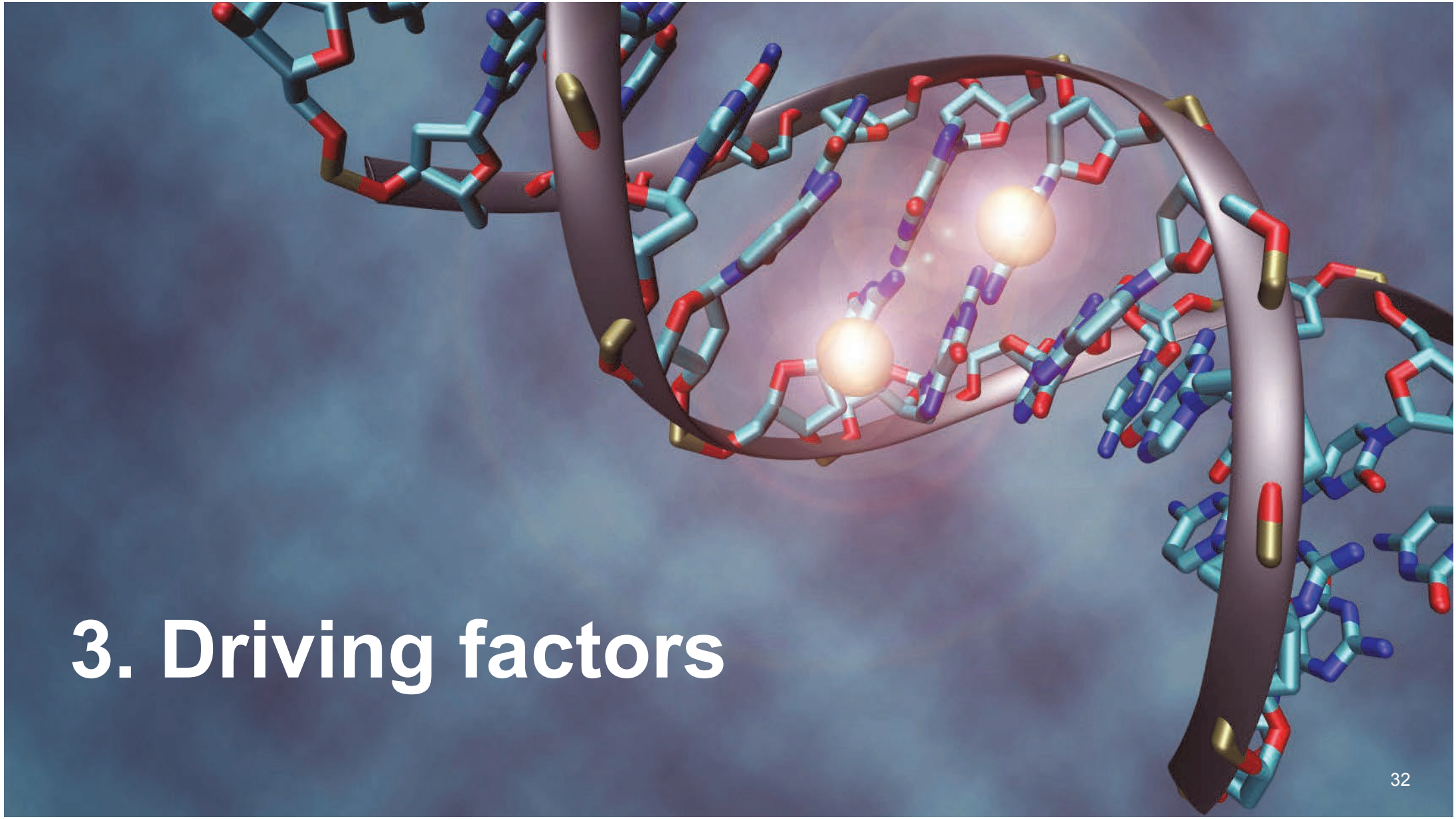
Both of these interactions upgrade the other sector’s value chain. This could be through the incorporation of a cheaper process, or could consist of the shortening of the value chain. For example, in the case of Oxford Biotrans’s grapefruit fragrance, the chain is shortened by the introduction of synthetic fragrance, as it does not need to be made naturally.

The synthetic value chain could operate in many sectors, but there are some constraining factors

Synthetic biology has possible applications in a wide variety of sectors. Currently it is most used in the pharmaceutical and fragrance and flavours sectors.

- The pharmaceutical sector was perceived by our interviewees to be the most willing to consider employing synthetic biology. This is highlighted by the fact that there are already a number of synthetic products on the market, such as synthetic insulin and synthetic artemisinin. Some of the reasons the pharmaceutical sector was thought to be more willing included:
    - There is a lower social risk as the benefits of drugs are clear to consumers.
    - The pharmaceutical sector is highly regulated and therefore they have experience in terms of regulatory requirements.
    - Due to the size and turnover of pharmaceutical companies they have the capacity to address investment risks, and the production capacities that smaller companies would not have.
- Food and agriculture sector companies were perceived to be less willing due to fears of social acceptability, and the stringency of regulatory frameworks. These factors have geographical implications. Most participants thought that it is more likely for US-based companies involved in the food and agriculture industry to adopt synthetic biology products rather than EU ones, as the EU is characterised by a more precautionary approach when it comes to food regulations.
- Due to size and organisational culture, it was perceived that large, end-user companies would have a *reluctance to change and adopt new techniques*. This reluctance could vary by sector and was thought to be highest in industries where the cost margin is very low. This means that the benefits of synthetic biology must be very clear for it to be a worthwhile risk to take on.

The amount of involvement of sectors in synthetic biology is also affected by the current economic viability of products in that sector. While large investments originally went into the promise of biofuels, and many start-ups started off with that product in mind, production of biofuels through synthetic biology has been largely unsuccessful due to difficulties producing sufficient quantities at a low enough price point to compete with traditional fuel. Organism design companies instead switched their focus to products where the price per kilogram is higher, the volumes required lower, and the margins much higher, such as flavours and fragrances. This switch allows companies to both make a profit and develop their processes, with an eye to realising returns down the line with very high volume products such as fuels.



3. Driving factors

Driving factors

Outline of section

In this section we present our analysis of the main driving factors that are currently, and could in future, affect the synthetic biology value chain and commercialisation opportunities. The drivers come from both the review of the literature and the interviews with stakeholders. We have organised the drivers according to a PESTLE framework, identifying whether they are a Political, Economic, Social, Technological, Legal or Environmental driver.

Main messages

- *Political* factors are driven by uncertainty over future regulation and the lack of coordinated international efforts.
- There are more *economic* factors affecting synthetic biology than others. It is considered a risky and expensive business by investors and there is a negative feedback loop that is difficult to break.
- The *social* factors likely to have an impact on the development of synthetic biology are associated with the social acceptability of synthetic biology products. The social acceptability is linked to the anticipated balance between benefits and perceived risks by the general public.
- *Technological* factors include the poor reproducibility of engineered organisms and poor interoperability of R&D protocols. This results in slow engineering processes and a perceived lack of scientific advancements.
- Synthetic biology companies and regulatory authorities view the nature of *legal* factors differently.
- The main *environmental* factors likely to have an impact on the development of synthetic biology are associated with the potential threat of released synthetic biology organisms on biodiversity and on human health.

What is a PESTLE framework?

A PESTLE framework was used to categorise the drivers of synthetic biology that were identified through the literature review and interviews. It is a commonly used analytical tool for categorising information about a range of different contextual issues that will influence any future environment. It helps in the analysis of the future as it provides a useful ‘checklist’ of the types of factors one might need to think about. For our purposes, it allows one to identify the main external factors and drivers that will impact the synthetic biology sector and evolution of the value chain.

The factors have been identified first by relying on the literature review. The interviews allowed us to validate and nuance these factors from the company perspective, as well as identify any new factors. Ultimately, unless otherwise noted, all factors identified in the following slides were found in both the literature and the interviews and so we can be relatively confident in the strength of the findings. Quotes are used for illustrative purposes only.

Political factors

Summary: The main political factors likely to have an impact on the development of synthetic biology are associated with:

- The existence of international regulations and standards (or lack thereof).

International political factors

The international nature of innovation and the global industries for which synthetic biology might be used means that coordination within and across countries is needed.

International cooperation for coordination of regulations is politically challenging as countries experience large differences in the stringency of regulations. This could make the adoption of international standards difficult [1]. For example, regulations for genetically modified organisms are less stringent in the US compared with the UK [2]. Additionally, countries experience large differences in their regulatory approaches, for instance the US has adopted product-based regulations to biotechnologies whereas European countries tend to have process-based regulations.

In terms of funding, international political cooperation to develop complementary synergistic programmes is lacking between countries that would provide mutual benefits and accelerated competitive leadership [3].

The lack of international and harmonised regulations might incentivise the movement of production facilities to countries that are less well regulated. This could foster an informal synthetic biology sector, which could have negative economic consequences and could impede the efforts of national authorities hoping to regulate the sector.

Political factors

Summary: The main political factors likely to have an impact on the development of synthetic biology are associated with:

- The level of national political support
- The influence of the national public opinion on the willingness of governments to make regulations.

National political factors

At the national level, the main political factors that might have an impact on the development of synthetic biology concern:

- Public attitudes towards genetic modification.
- Political desire to maintain a competitive advantage.
- Local or national regulations that might discourage the growth of the sector and/or encourage the sector to move to less well regulated countries.
- National support for research and development.

Internal political support differs depending on countries. According to various interviewees (from both the UK and the US), internal political support is stronger in the UK than in the US [1]. This helps in various ways. One UK interviewee noted that UK national authorities have better engagement with national regulatory bodies, which makes policy change more likely in the UK [2]. Government support (in terms of funding and infrastructure for instance) could also help to reduce market failures, notably by easing the entry of companies into the market of synthetic biology [3].

Governments might also be reluctant to introduce regulations for the synthetic biology sector due to the potential lack of public acceptability of the technology. On the other hand, as one interviewee noted, social awareness can be an important driver for establishing regulations for the industry [4].

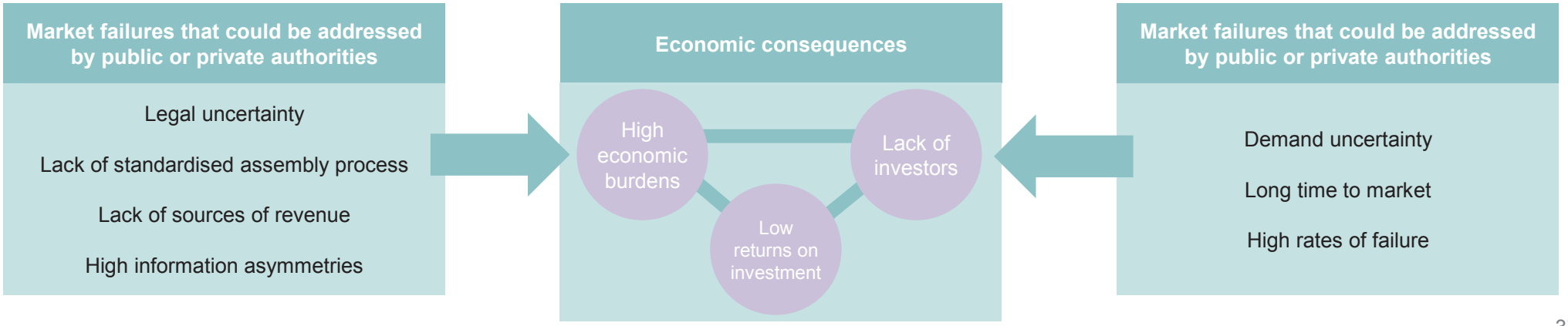
Economic factors

Summary: The main economic factors likely to have an impact on the development of synthetic biology are associated with:

- The perception of risk inherent in synthetic biology by investors
- The availability of funding and sources of revenue for companies and their ability to generate value
- High transactional costs
- Uncertainty about the level of return on investment.

Synthetic biology is considered a risky and expensive business by investors and there is a negative feedback loop that is difficult to break.

- This is due to long development times and potentially high rates of failure associated with the development of a product [1]. This is in contrast to more traditional venture capital, where there is a relatively short development time needed for successful launch of companies (e.g. software companies).
- There is a risk that synthetic biology will be unable to demonstrate an acceptable proximity to market and there will be limited mechanisms for return on investment due to the lack of funding organisations that would be able to support precompetitive research [2].
- This uncertainty and risk is reinforced by the uncertainty around the acceptance and demand for synthetic biology products by the general public [3] and around the willingness of 'big customer companies' to buy and integrate synthetic biology processes [4]. As one interviewee commented, '*established businesses have somewhat of a resistance to change*' [5].



Economic factors

Summary: The main economic factors likely to have an impact on the development of synthetic biology are associated with:

- The risk perception of synthetic biology by investors
- The availability of funding and sources of revenue for companies and their ability to generate value
- The level of transactional costs
- The level of return on investment.

While the negative feedback loop of investment is one of the main economic factors, there are several others that could influence the future of synthetic biology:

- **Sustainability of funding and high economic burdens weigh on the shoulders of synthetic biology companies, especially SMEs.** Their survival depends on their ability to generate a steady revenue stream that covers the big investments being made in R&D as well as their ability to create value. However, they encounter difficulties in maintaining their revenue stream and identifying new sources of revenue [1].
- **High transactional costs are associated with the lack of standardised assembly processes as well as with regulatory uncertainty.** There is a lack of predictability of timeframes for review [2] as well as the need for extensive work to ensure compliance with existing regulations (and potential future regulations).
- **Synthetic biology companies are thought to experience low return on investment at present.** The cost of developing a new organism that could lead to a new product requires heavy investments, which may outweigh the return on investment. Moreover, investors may be wary due to the lack of examples of industrial biotechnology companies having a tremendous financial success [3]. Additionally, it takes several years to generate any revenue [4]. The heavy investments in manufacturing equipment associated with the need for companies to scale up constitute a high barrier to entry on the market [5].

  'Even if you are making a molecule that is chemically identical to a molecule that is already in a existing product, it still takes 2 to 3 years for that product to be accepted, that's a long time to wait!' [6]

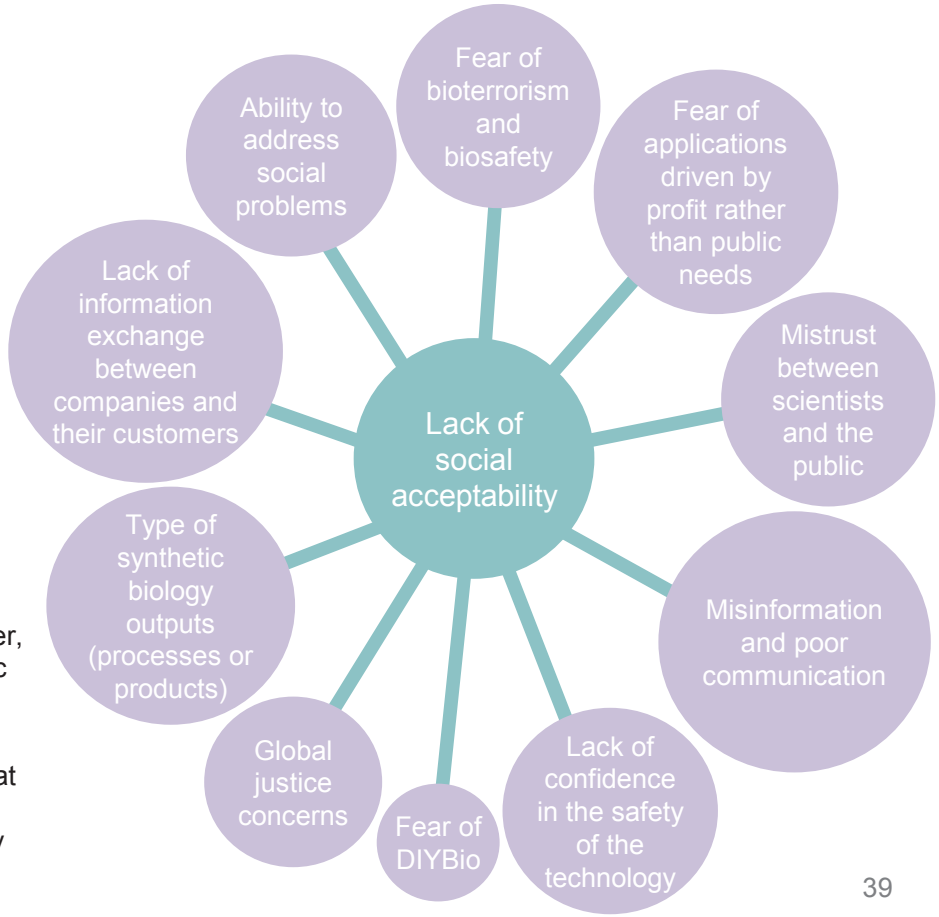
- The weight of these economic factors will depend on the type of synthetic biology companies; companies selling synthetic biology products may bear a higher economic burden than organism development companies, which are process-oriented [7].
- Finally, there were two additional points raised in the literature, but which were not also raised by interviewees. First, there is thought to be a lack of human capital to meet the needs of the industry. There is a need for training to increase awareness and skills, particularly if synthetic biology is to help drive the bio-economy [8]. Second, at the macro level, the adoption of synthetic biology could lead to affordability issues; for instance, the use of biofuels by transforming the car industry could lead to increasing prices in this industry [9]. Additionally, large corporations could create monopolies, which could reinforce the role of traditional actors in the value chain [10].

Social factors

Summary: The main social factors likely to have an impact on the development of synthetic biology are associated with the social acceptability of synthetic biology products, which depends on several factors.

The social acceptability of synthetic biology products is linked to the anticipated balance between benefits and perceived risks by the general public. Social acceptability is likely to be influenced by several factors:

- The **fear of bioterrorism and biosafety** and of **applications driven by profit** rather than public needs [1].
- The **mistrust between scientists and the general public**. This comes from the fear that scientists focus on the positive outcomes of synthetic biology, and miss the potential risks, or take short cuts [2]. There is the risk of a disconnect between individuals' own research, which can be seen as incremental or routine, and the perception by the general public, which can see it as transformative [3].
- The **poor communication** around the actual benefits of synthetic biology, which may hinder social awareness [4]. The term 'genetic engineering' might constitute a barrier to public acceptability [5].
- **The lack of exchange of information between companies and their customers** reinforces the feeling of mistrust and the poor understanding of the public about what synthetic biology is and its potential benefits [6].
- **The type of synthetic biology outputs and areas of application**. Social acceptability is likely to be more stringent regarding synthetic biology products than synthetic biology processes used to make products that are not themselves genetically engineered. However, social acceptability may be greater if it was thought synthetic biology was creating a 'public good' or could address societal problems [7].
- **Finally, though not raised in the interviews, there are ethical concerns** regarding the 'biohacker' community and 'DIYBio' synthetic biology activity [8], as well as perceptions that synthetic biology may contribute to **rising inequality** between developed and developing countries. If synthetic biology allows for replacement products from those that are currently produced in developing countries, there may be issues of global justice at play [9].



Technological factors

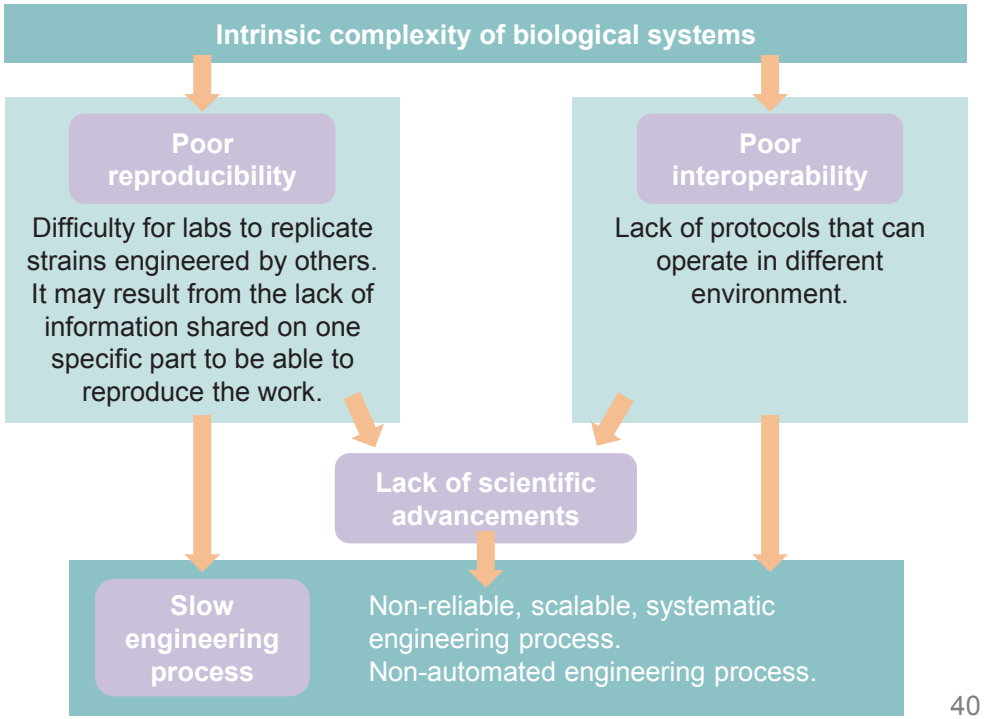
Technological challenges associated with the development of synthetic biology come from the '**intrinsic complexity, nonlinearity, diversity and evolutionary capacity of biological systems**' [1]. This leads to poor reproducibility and poor interoperability, which impede the proper exchange of information and generate high costs and poor productivity [2]. Companies may have their own research and development process and codified names. This makes the exchange of knowledge and services with partners and suppliers more difficult as they do not speak the same language. All of this could explain the lack of scientific advancements and of common understanding of the issue [3], as well as the slow engineering processes and the difficulty to implement an automated, scalable and systematic process.

> *'The current state of the art is not up to turning biology into engineering. […] You can design genetic circuits but times out of 10, they do not work.' [4]*

> *'We need to get a lot better and faster engineering biology in order to start generating successes.' [5]*

Summary: The main technological factors likely to have an impact on the development of synthetic biology are associated with:

- The poor reproducibility of engineered organisms and poor interoperability of R&D protocols due to the intrinsic complexity of biological systems.
- The slow engineering process resulting from poor reproducibility and interoperability and from the lack of scientific advancements.



Legal factors

Summary: The main legal factors likely to have an impact on the development of synthetic biology are:

For synthetic biology companies:

- The technical challenges for companies to comply to standards and regulations
- The risk that regulations would impede synthetic biology companies to scale up and to diversify
- The time and costs associated with respecting intellectual property rights.

Synthetic biology companies perspective

Technical challenges

- Environmental and safety approvals [1].
- Regulatory hurdles especially linked to organisms released in
- the environment [2].
- Rules around containment [3].
- Nagoya Protocol [4].
- Different regulations/certifications to obtain and comply with depending on the geographical area [5].
- Different regulations depending on the industry (more stringent for instance in the agro-food and consumers products industries according to some interviewees) [6].

Intellectual property (IP)

- IP can lead to time and costs associated with material transfer agreements from universities [7].
- Large royalties could be made by those who hold IP, but this could make it difficult to build on existing knowledge if proprietary IP is kept specific to companies [8].

Legal factors

Summary: The main legal factors likely to have an impact on the development of synthetic biology are:

For regulatory authorities:

- The technical challenges associated with developing appropriate standards and regulations
- The risk that too strict regulations would restrict R&D, innovation and economic growth
- The need for the right balance of intellectual property protection and openness to enable collaboration.

Regulatory authorities perspective

Technical challenges

- Difficult to determine whether the synthetic biology products fall under deliberate release or contained use regulations [1].
- Difficulty in performing risk assessments [2].
- Lack of adequacy of current regulatory systems to monitor progress across countries [3].
- Challenges associated with standardising the intrinsic complexity of biological systems [4].
- Regulation of synthetic biology at its early stage may mean regulation of risks associated with research, not with products and future innovation.
- Regulations need to reflect the best scientific understanding of the technology [5].

Intellectual property (IP)

- Need some form of protection of intellectual property without jeopardising the necessary openness to progress [6].
- Patents could allow more knowledge to be available for further research and the lack of intellectual property mechanisms could hinder the release of new knowledge; however, there is a question as to what should be patented [7].

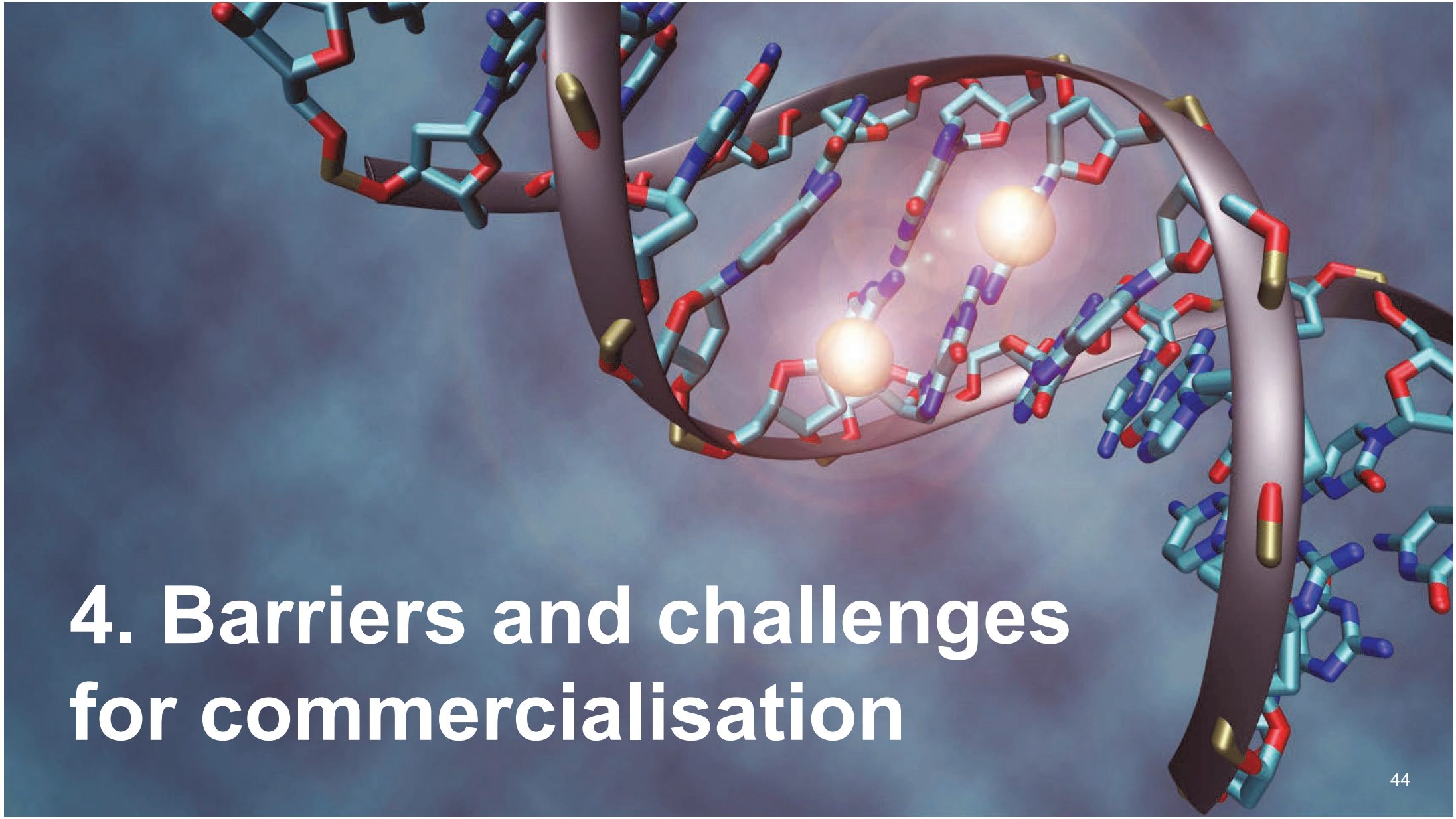
Environmental factors

Summary: The main environmental factors likely to have an impact on the development of synthetic biology are associated with the potential threat of released synthetic biology organisms on biodiversity and on human health.

Synthetic biology may pose a number of threats to the environment, including:

- The release of synthetic biology organisms into the environment could lead to cross-contamination or pesticide resistance [1].
- Concerns have arisen that an escaping organism could threaten ecosystems and that synthetic biology could lead to less biodiversity in the long run [2].
- Synthetic food could limit the availability of organic and conventional crops [3].
- There could be a risk to public health if previously eradicated pathogens are reintroduced into the ecosystem [4].

> *'In biology there is a perception that everything is alive and can take over.' [5]*
>
> *'A challenge would be with organisms that are intentionally released in the environment.' [6]*
>
> *'As synthetic biology tools become better and better, our ability to change an organism from what it was into something radically different increases as well as concerns around containment.' [7]*



4. Barriers and challenges for commercialisation

Barriers and challenges for commercialisation

Outline of section

This section discusses the barriers and challenges for commercialisation of synthetic biology products, as perceived by the stakeholder interviewees. We differentiate how each of these barriers and challenges differed between companies by presenting the findings along different stages of the value chain.

Main messages

- The barriers and challenges expressed by the interviewees have been mapped along the value chain, thereby providing a way to differentiate between companies that links to our overall analysis.
- There are three main challenges identified at the *idea stage*: i) the current level of scientific knowledge makes it hard to make the most of what synthetic biology promises; ii) there is a reluctance/inertia of established companies to change and adopt synthetic biology; and iii) there is a lack of communication and understanding between industry and academia and a poor exchange of information between different companies.
- At the *design-build-test stage* the following barriers are thought to exist: i) the current level of scientific knowledge; ii) poor exchange of information; iii) lack of integration and innovation around equipment; and iv) intellectual property rights.
- The most numerous barriers and challenges emerged at the *scale-up stage*:
  i) reluctance/inertia of companies to change; ii) difficulties in maintaining a revenue stream; iii) lack of a notable financial success; iv) regulatory hurdles; v) the level of scale up required to have a good return on investment; vi) negative public perception; vii) concerns about environmental release; and viii) intellectual property rights.
- The size of the market in the US and the nature of private investment meant there was slightly less concern about investment related to scale up among US companies than among UK companies.

Barriers and challenges for commercialisation vary depending on the stage of the value chain

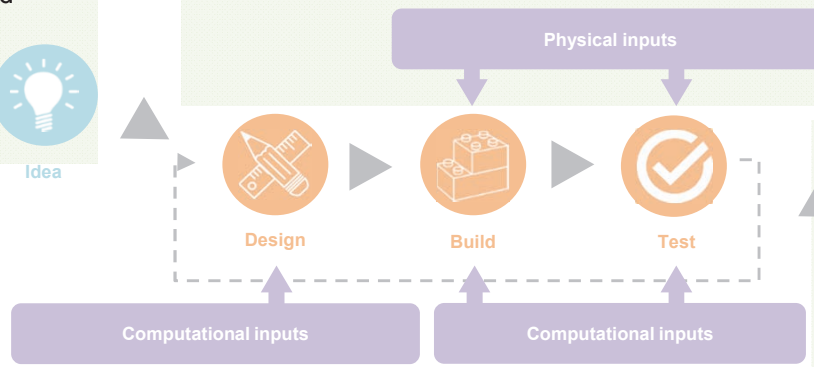
In the following slides we describe how interviewees thought about different barriers and challenges affecting commercialisation opportunities for synthetic biology. We have presented these findings according to the different stages of the value chain in order to show how they vary by company and across sectors.

Barriers or challenges – **Idea stage**

- Current level of scientific knowledge
- Reluctance/inertia of companies to change
- Lack of understanding between industry and academia
- Poor exchange of information

Barriers or challenges – **Design, build and test stage**

- The current level of scientific knowledge
- Poor exchange of information
- Lack of integration and innovation around equipment
- Intellectual Property Rights



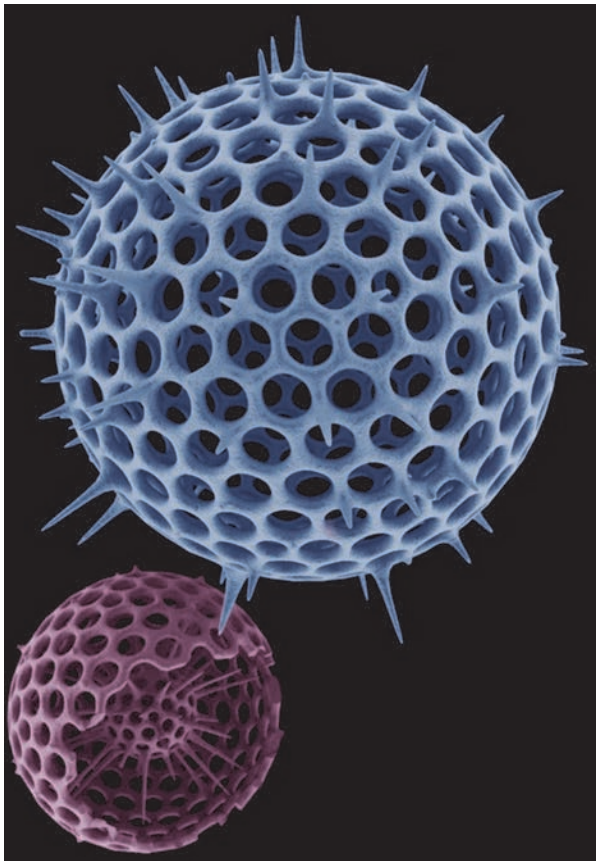
Barriers or challenges – **Scale up/integration into other industries stage**

- Reluctance/inertia of companies to change
- Maintaining a revenue stream
- A lack of notable financial success
- Regulatory hurdles
- The level of scale up required
- Public perception
- Environmental problems

Barriers and challenges at the idea stage

Four main barriers were identified as causing challenges in the *idea stage* of the value chain:

- A key technological barrier to commercialisation of synthetic biology, is the **current level of scientific knowledge**. The majority of interviewees mentioned a 10 year timeline for the arrival to market of disruptive innovative products. This technological barrier would be expected to decrease over time
- The **reluctance/inertia of established companies to change** means that companies, particularly large established companies, need to see a significant benefit in order to consider adopting synthetic biology products or processes. It was suggested that this inertia may mean that established companies will wait for smaller companies to develop products of interest to them, and then acquire either the company or a licence for the product, rather than carrying out the research themselves.
- The idea stage was felt to be limited by a **lack of communication and understanding between industry and academia**. It was perceived that academics don't understand industry's needs and that the research that comes out of universities cannot necessarily be immediately transferred in order to answer private sector problems.
- Related to the above point, synthetic biology start-ups, which are generally 'Business to Business' companies rather than 'Business to Consumer' companies, raised concern that there can be **poor exchange of information** between them and their providers. This can limit the ideas that companies decide to work on and was raised as an issue by both companies that would demand these services and the ones that would provide them.



Barriers and challenges at the design-build-test stage

The *design-build-test cycle* is the core research process of synthetic biology. Four main barriers were identified by stakeholders as causing challenges in this stage of the value chain:

- As before, the **current level of scientific knowledge**, and lack of scientific advancements in some areas, can slow down this stage of the process as there is an in-built limit to how far scientific knowledge can take us at this stage.
- **Poor exchange of information** between synthetic biology start-ups and their providers can slow down the design-build-test cycle.
- As experiments are expensive to run and often require several types of equipment the **lack of integration and innovation around equipment** can lead to high costs and therefore acts as an economic disincentive. This particularly affects established companies who already have equipment to perform their normal processes, and may not have the available investment to upgrade their equipment.
- These steps in the value chain generally involve input from several stakeholders. Protection and ownership of **intellectual property rights** was seen to be important by a range of participants from both the US and the UK. A particular issue raised was that when contracting the services of universities to work on certain projects, companies face long negotiations about patent rights and even the prospect of not being able to use the end result due to these considerations. This further highlights the divide between industry and academia, which can make it difficult for industry to take advantage of the knowledge base at universities.

Barriers and challenges at the scale-up stage

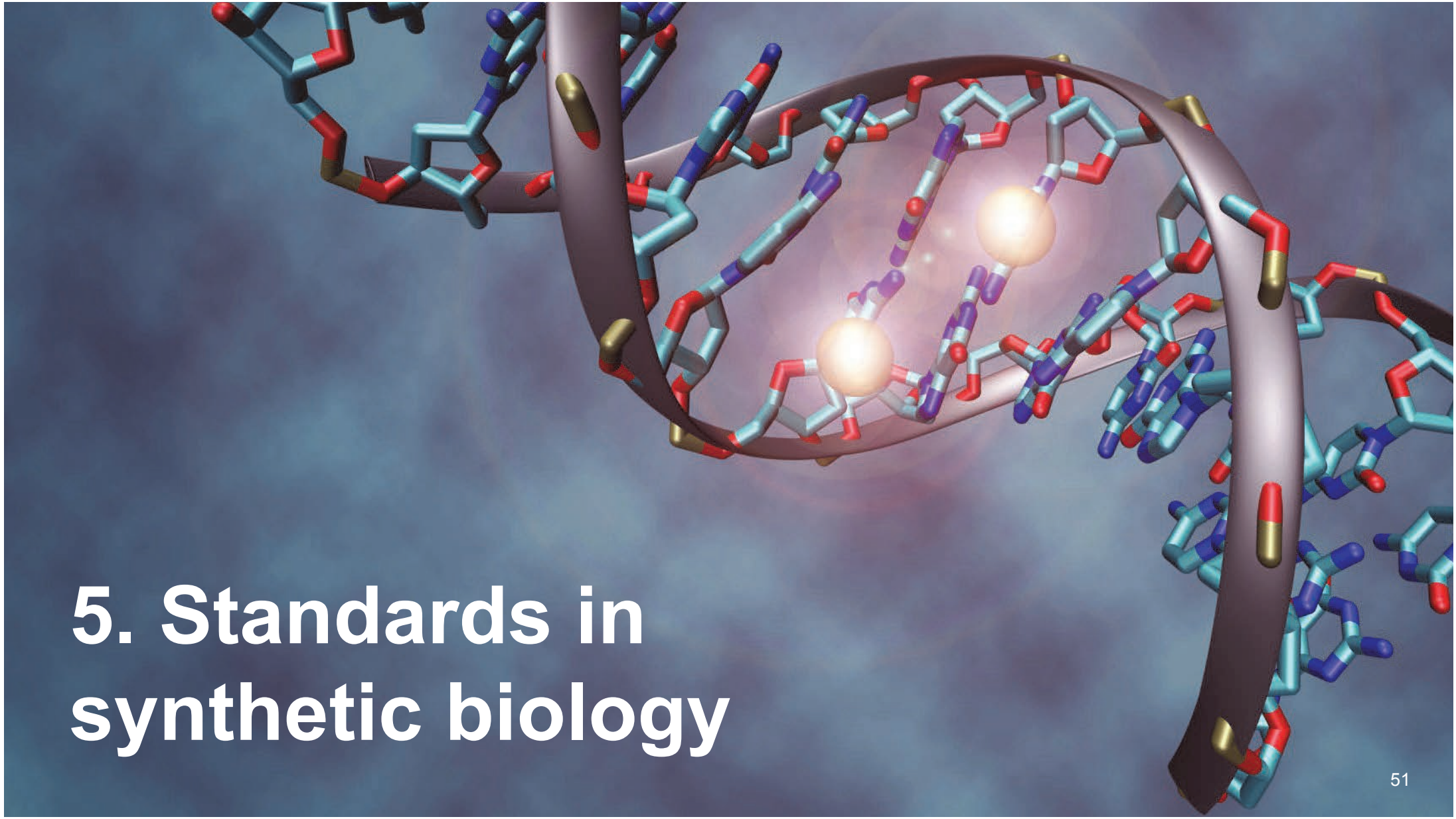
Stakeholders identified the most challenges for commercialisation at the *scale-up stage*. This was the case both for start-ups and for end-users.

Stakeholders identified the most challenges for commercialisation at the *scale-up stage*.

- As the business model for many synthetic biology start-ups is to design organisms and then sell this organism to large sector-specific companies, the sector-specific companies are the ones responsible for scaling-up the product to required levels. **The reluctance/inertia of these companies to change** may affect their willingness to take on this step.
- One reason for many start-ups selling the organisms they have developed before the scale-up stage is the difficulty in **maintaining a revenue stream** that will allow for them to scale up and produce their product. Interviewees from the US and the UK noted that there is little state funding for this development stage. The financing for scaling up therefore needs to be supported by private investors. This problem is not unique to synthetic biology.
- **A lack of a notable financial success** from synthetic biology may affect the likelihood of both outside investors and established companies investing in synthetic biology. Interviewees highlighted the differences between the US and UK in terms of private investors. The US market size as well as the existence of business and technology hubs such as San Francisco, San Diego or Boston and New York were seen as advantages. It was also mentioned that the US has a more risk-taking culture, which could help synthetic biology companies access more capital. When referring to state support, interviewees expressed advantages for both the US and the UK. Within the US there is the significant financing towards development of products using synthetic biology from the Defense Advanced Research Projects Agency (DARPA). However, UK interviewees commented on the government's specific aim to support synthetic biology as well as the ease with which one can engage with regulatory bodies.
- **Regulatory hurdles** can affect both the sectors synthetic biology is involved in, and the countries in which companies operate. One interviewee gave an example of a synthetic biology company that moved its production capacities outside the US and the EU to a country where there was an unclear regulatory framework. While this initially posed a barrier, the company supported the local government in setting up legislation in this field and can now take advantage of favourable regulation and lower production costs. This example raises important questions about the global governance of value chains in the future and highlights the role standards might play if coordinated international regulation becomes untenable.

Barriers and challenges at the scale-up stage

- **The level of scale up required** affects the sectors involved in synthetic biology. This is particularly clear for the biofuels sector where synthetic biology applications can show promise. However, commercialisation of these products would need to entail large volumes and low production costs in order to make a profit. Achieving such economies of scale is an important component of industrial scale up and realisation of commercial returns. The fact that production costs are still high means there is a perception that this industry is not one where synthetic biology applications are going to be widely adopted in the near future.
- **Public perception**, and the benefit the public perceive they are getting from using a synthetic biology product over a 'traditional' product, will also affect which sectors are able (or willing) to scale up synthetic biology products and integrate them into existing value chains. Interviewees described the pharmaceutical sector as being willing to take on synthetic biology risks as the benefit to consumers of new curative drugs are very clear. Applications in agriculture, food or cosmetics, however, are examples where the benefit may fall more within the value chain (and hence to industry), rather than reaching the consumer. Hence, the consumer may not necessarily see the benefit, but they will see the risk. These sectors are less likely to benefit from synthetic biology in the short term.
- The potential **environmental release** of synthetic biology products is a barrier to scaling up and is particularly relevant for the food and agriculture industries, where there is a perceived potential of organisms to be spread out into the environment and cause unintended changes to the ecosystem. The fear is exacerbated by the perceived risk that 'Do It Yourself (DIY)' kits could enable the wider public to produce and release such organisms.
- Similar to the design, build and test stage, the ownership of **intellectual property rights** can affect also the scale up and integration of synthetic biology into other industries.



5. Standards in synthetic biology

Standards in synthetic biology

Outline of section

Given the barriers and challenges just identified, this section describes how standards could help develop the market in synthetic biology. We discuss the benefits of standards at different stages of the value chain, as well as highlighting some of the challenges of developing standards. All findings are based on the stakeholder interviews.

Core messages

- At the *idea stage* standards could give weight to the field and help establish it as a defined field. They could also improve communication within the community and help to bridge different sectors by providing a common vocabulary. Technical standards could resolve some of the problems that currently require firms to expend resources by providing specifications for input and output values.
- At the *design-build-test stage* standards could: i) help with the interoperability of the equipment and improve the workflow with providers and buyers and ii) enable innovation by facilitating competition between and within technologies. Open standards were thought to be important for facilitating superior IP for end-products.
- At the *scale-up stage*, standards could improve the efficiency of regulatory processes; allow for reproducibility and reduced transaction costs, thereby allowing greater productivity; enable the emergence of innovative products; increase trust; and address environmental containment concerns.
- The interviewees also highlighted several challenges and concerns with standard setting. While the overall opinion on standards was positive, they cannot be considered the solution to every problem in synthetic biology, and there will be instances where they could block innovation or render the activities of some companies obsolete.

How could standards help develop the market in synthetic biology?

There are many barriers to the successful translation of ideas from the laboratory into the marketplace. This is where the role of standards can come in and there are many ways in which the literature suggests standards could have an impact on innovation [1, 2]:

- Contribute to a coherent response, as well as build a critical mass in the early stages of technology and market development.
- Build customer trust – in particular standards for measurements and tests, by demonstrating that the innovative products have attained an acceptable level of risks for health safety and the environment.
- Classify and disseminate state-of-the art and best practices in science and technology.
- Facilitate competition between and within technologies, contributing to innovation-led growth.

In addition to supporting innovation, standards can make a positive contribution by helping to ensure good communication, compatibility, interchangeability, reproducibility, effective use, fitness for use, safety, quality assurance, consumer protection and environmental protection.

Within synthetic biology, standards could help overcome, or lower some of the barriers and challenges companies are facing. However there are challenges that standards pose. These two elements are presented on the next two slides. The slides contain the analysis of the views participants expressed on these aspects. While the research was focused on gathering the diversity of perspectives, the tables offer insight into the relative strength of evidence behind each point. There are three levels of shading – the lightest one expresses a minority view (fewer than four interviewees) while the strongest shading indicates an opinion that came through prominently.

It is worth nothing that the number of barriers and challenges mentioned, as well as the relative importance of standards, was dependent on the position the company had in the value chain. For example, one company that provides mostly physical inputs mentioned two barriers: poor exchange of information and regulatory hurdles as these were the ones that were important from their point of view. There may have been other barriers if we had provided a list, but these were the two at the forefront of their thinking. It is also important to note that the mapping of the value chain was performed after most of the interviews took place and therefore the categorisation across the stages of the value chain was based on our interpretation and analysis.

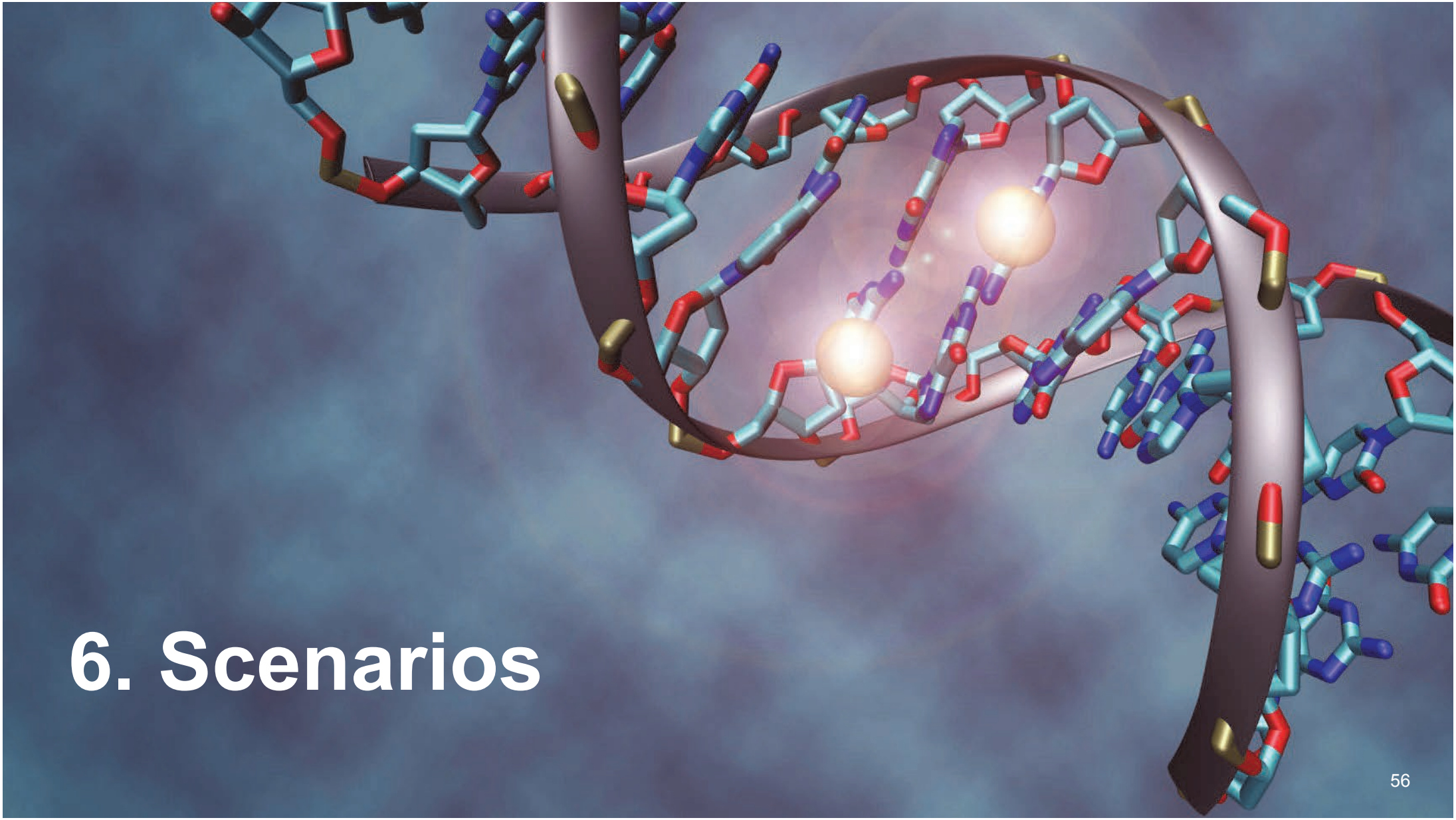
Nevertheless, we can say with confidence that overall the majority of participants expressed that standards can help with commercialisation in various ways. However, they did not offer reflections on specific technical details of such standards.

Potential benefits of standards

	Barrier/Challenge	Strength of evidence	Potential benefits of standards	Strength of evidence
Idea stage	Reluctance of considering synthetic biology at the idea stage due to scale up and regulatory hurdles	*(majority)*	Standards could help with the production capacities as well as with simplifying the regulatory process.	
	Reluctance or inertia of companies to change and adopt new techniques	*(mid-range)*	Standards could give weight to the field by contributing to it being perceived not only as an interesting domain but one that is becoming more and more defined. However, this will require a cultural change and while standards will support the transition, they should not be expected to lead the change.	
	Disconnect in understanding the industry needs by academia		Standards could improve communication in the synthetic biology community and bridge different sectors.	
	Poor exchange of information	*(minority)*	Classifying type of standards that will provide definitions towards a common vocabulary.	
	Insufficient scientific advancements		Technical standards could resolve some of the problems that currently take out resources by providing specifications for input and output values. This will enable concentration of efforts in other scientific directions.	
Design-build-test	Lack of integration around equipment		Standards could help with the interoperability of the equipment and improve the workflow with providers and buyers.	
	Lack of innovation around equipment		Standards can enable innovation by facilitating competition between and within technologies, therefore contributing to innovation-led growth.	*This point is in the literature.*
	Intellectual property rights		Open standards can facilitate superior IPR for end-products.	
Scale-up	Lack of understanding of synthetic biology problems		Standards could facilitate better understanding of the field by a less technical person.	
	Regulatory issues		Standards could simplify the documentation necessary for review by some competent authorities and reduce the review time associated with these processes.	
	Necessity to scale up		Standards could allow reproducibility and reduce transaction costs therefore allowing greater productivity.	
	Lack of a notable financial success		Standards have the potential to enable emergence of innovative products, which in turn could lead to financial successes.	
	Need to attract investors		Standards could increase trust for private investors.	
	Negative public perception		Standards could increase public trust. These type of standards could be ‘soft’ standards like a code of ethics.	
	Environmental release concerns		Standards could help mitigate this risk by having clear containment requirements.	

Potential challenges in developing standards

Process stage of standard development	Challenges	Strength of evidence
Formulating standards	The scientific complexity of biology increases the difficulty of standardisation.	
	Items or topics for standardisation must be chosen carefully in order to avoid stifling innovation by forcing technological lock-in.	*This point is in the literature.*
	Standards need to be specific so that they are widely understood and can be widely adopted.	
	Standards that are useful for industry may not be the same, or align with those that are useful for academics.	
	There are few academic incentives for formulating standards as developing standards does not tend to lead to academic recognition such as publications or accessing research funding.	
	Standards are more likely to be implemented if they are the result of a collaborative effort. This can be difficult to achieve, particularly with a global community.	
Adopting standards	It is harder to ensure adoption of standards than it is to formulate them. Ensuring standards add value encourages their adoption.	
Long-term impact	The timing of standards is important. Premature standardisation could lead to stifling of innovation, whereas late standardisation could risk missed opportunities.	*This point is in the literature.*
	Due to the nature of synthetic biology, standards chosen now may have only a brief utility. This could deter individuals from engaging in standard setting.	
	The degree of impact that standards bring is dependent on the position the activity has in the value chain. Some companies' activities could be rendered obsolete by the introduction of standards.	



6. Scenarios

Standards in synthetic biology

Outline of section

This section describes four different scenarios that were used to explore future opportunities for synthetic biology and to test which actions might be needed to allow us to maximise these opportunities. The scenarios were developed during an internal workshop with the project team, BSI and four senior advisors. We provide an overview of the four scenarios and then discuss how they can be used to draw out lessons for this study.

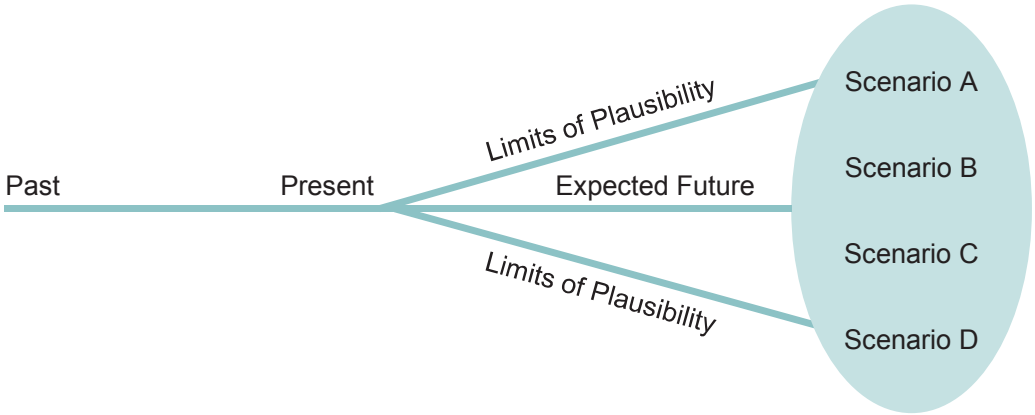
Core messages

- Four scenarios were developed and used to test the future:
    1. *Catastrophe leads to containment* presents a future characterised by a very conservative regulatory environment.
    2. *Synthetic biology for the public good* envisages that the synthetic biology value chain is driven by a need to develop goods and services that serve the public good.
    3. *Synthetic biology and the 'entrepreneurial state'* proposes a synthetic biology value chain driven by high financial investment from the state.
    4. *The sharing economy model* proposes a space dominated by many specialised smaller companies.
- The scenarios bring out several facets that standards and regulations, as well as public sector versus private sector investments, can play. They highlight the different degrees to which sectors can cope with synthetic biology challenges, for example pharmaceutical companies are better placed to overcome barriers.

Using scenarios to explore the future

Why have we used scenarios?

A scenario is a logical and consistent picture of the future that is not only credible, but also challenging in important respects. It is a means of stimulating deeper conversations about the future direction of a certain policy or innovation area. Building scenarios is therefore an exercise in both discipline and creativity.



The discipline is needed to structure the set of scenarios so that they reflect the issues requiring exploration. Creativity is needed in filling out the scenarios so that they become meaningful, consistent and plausible. Scenarios are deliberately meant to test the limits of plausibility and so may not be 'realistic' in a conventional sense, but should challenge thinking. One of the key elements of scenarios-based analysis is understanding the implications of uncertainties and likely impacts.

How are we bringing scenarios and the synthetic biology value chain together?

We developed a series of possible scenarios for the future evolution of the synthetic biology sector, using the year 2026 as our future reference point. The scenarios were developed during an internal workshop on the basis of a subset of the PESTLE factors described above. The subset was determined on the basis of which factors were likely to have a high impact on commercialisation and very likely to occur, as well as having those that standards were likely to be able to influence. This mapping is presented in Annex 5.

The basis for the scenarios was created during the workshop and then further fleshed out in subsequent internal discussions. They contain detail about different factors that might shape, enable and constrain the evolution of the value chain, as well as reflect different governance approaches and sets of standards that could be used to influence the value chain(s).

We then tested these scenarios with seven stakeholders who had been interviewed previously in the study. The opportunities, uncertainties and risks presented after each scenario reflect the discussions that took place witwith the stakeholders about the potential plausibility and implications of each scenario, as well as our own further analysis.

Scenario 1: Catastrophe leads to containment

Summary table	
Main driving factor	Public opinion – negative public opinion about synthetic biology and high perceived risks.
Configuration of value chain	Dominated by big firms able to comply with restrictive and onerous standards.
Nature of innovative activity	Incremental innovation.
Nature of investments	Likely to rely on big companies' internal investment as it would be too risky for external investors to invest in smaller companies.
Outputs of synthetic biology	Companies selling processes to other companies; no 'products' reach end users.
Interplay between regulations and standards (types of standards)	Likely to have highly restrictive regulations and standards notably to enforce strict containment practices. Standards would include: • Strict standards on biological containment • Standards around measurement (e.g. purity of samples) • Standards for training to manipulate and handle synthetic biology organisms • Standards that develop a framework for responsible innovation.
Nature of intellectual property	Difficult to determine as we have no 'products' of synthetic biology.

Scenario 1: Catastrophe leads to containment

Driven by a negative public opinion of synthetic biology

How did we get here?

A very conservative regulatory environment is in place as a result of an extreme event that has resulted in an adverse, public reaction to synthetic biology. The value chain is driven by the need to constrain the use of synthetic biology. In this case, companies are only selling processes to other companies and no synthetic biology products reach the end-users. The value chain is dominated by big companies that have the financial resources to comply with highly restrictive regulations and would use synthetic biology as a means to achieve cost efficiencies, rather than as a strategy to enter new markets.

What are the opportunities?

- Though the scenario may start with very strict standards, over time the situation may improve and public trust may grow as a result of demonstrating how the sector can contain products. Thus, the ability to clearly build in appropriate safety mechanisms from the beginning could help will be critical.
- This scenario would push companies to focus on delivering products that had a value to society.
- A large amount of regulation would require countries to figure out how to balance regulation with economic growth. *'The first country to make regulation efficient will reap the benefits and get economic growth.'* [1]

Dominated by big firms

Characterised by incremental innovations

Guided by restrictive regulations and standards

Scenario 1: Catastrophe leads to containment

Driven by a negative public opinion of synthetic biology

What are the risks?

- You might end up in a highly regulated world, even without a 'catastrophic' event. *'We wouldn't need something bad to happen to end up in a highly regulated big industry sort of world.'* [1]
- Many interviewees commented that this scenario had already happened in other areas (GMOs and pharmaceuticals/drug manufacturing) and this meant that in some ways it was likely to happen again with synthetic biology, although in other ways it could also be less likely as we have learned from the past.
- Some countries just completely disregard the regulations, even if they are in place.
- Could end up with many companies owning all the patents and then no one else could get in.
- In any situation where there are high regulatory burdens you stifle the growth of small companies because only large companies can afford to be a part of it. *'This scenario becomes more likely in a capitalist society where small companies with good aspirations get taken over by large companies.'* [1]

Guided by restrictive regulations and standards

Results in processes rather than end-products

Scenario 2: Synthetic biology for the public good

Summary table	
Main driving factor	Public opinion – positive public opinion about the social benefits synthetic biology can deliver.
Configuration of value chain	Dominated by small, mobile companies that can quickly respond to public and societal needs.
Nature of innovative activity	Likelihood for disruptive innovations to emerge.
Nature of investments	Likely to have many public private partnerships as the main investment model, as well as significant amounts of public investment because of the need to align with government policy.
Outputs of synthetic biology	Mostly products that provide a societal benefit.
Interplay between regulations and standards (types of standards)	Close relationship between government policy priorities and standards development. Likely to have fewer regulations in order to support fast moving, emergent technology environment. Standards would include: • High technical/scientific standards to maintain positive image of synthetic biology and uphold public trust (in the absence of strong regulations). • Norms that incentivise companies to work with the public and NGOs to determine priorities for investment and directions of research. • Maintaining the positive nature of synthetic biology. • Environmental/containment standards would be strong. • Sustainable production.
Nature of intellectual property	Open source intellectual property.

Scenario 2: Synthetic biology for the public good

Driven by a positive public opinion

How did we get there?

Driven by a need to develop and sustain positive public opinion, the synthetic biology value chain is driven by the development of goods and services that serve the public good. There is deep trust and positive public opinion about the potential and ability of synthetic biology to deliver socially responsible and beneficial innovations, e.g. environmentally friendly detergents, vaccines, genetically engineered mosquitoes, diagnostic tools to help with AMR, synthetic milk to help prevent childhood diarrhoea, etc. In this scenario, small, mobile and nimble companies would be encouraged because they could respond more quickly to emerging societal needs (as compared with large multinationals).

What are the opportunities?

- Delivering sustainable social benefits from science. *'This is the dream. That's why we all do this.'* [1]
- Creating a way for IP to be held by smaller companies, such as open source IP, and avoiding traditional IP problems of pricing smaller players out of the industry.

What are the risks?

- Difficult to regulate, while also creating a situation for small companies where any sort of compliance/regulation was impossible.
- Could lead to unregulated lobbying.
- Open source IP doesn't work.
- Inevitably large companies would need to play a role. *'We start with good intentions, but things developed in the public good always end up commercialised.'* [2]

Dominated by small, mobile companies

Characterised by disruptive innovations

Opportunities for Public–Private Partnerships

Supported by public funding

Results in products with social benefit

Scenario 3: Synthetic biology and the ‘entrepreneurial state’

Summary table	
Main driving factors	Highly precautionary environment results in a need for high financial investment by the state to drive synthetic biology forwards.
Configuration of value chain	It could represent a combination of start-up companies as well as traditional players in fields that promise a high return on investment.
Nature of innovative activity	Mostly incremental innovations.
Nature of investments	The scenario would imply high regulatory costs but also high financial investment from the state in the areas of basic R&D and translation.
Outputs of synthetic biology	Due to high regulatory costs, synthetic biology would be used mostly in sectors that already have high regulatory demands, such as pharmaceuticals.
Interplay between regulations and standards (types of standards)	Standards development would be prioritised in an effort to smooth the regulatory process. Likely to have many standards that would address safety concerns. Standards would include: • High technical/scientific standards to ensure accuracy of synthetic biology manufacturing processes • Environmental/containment standards • Metrology standards for repeatable processes.
Nature of intellectual property	Patent protection.

Scenario 3: Synthetic biology and the ‘entrepreneurial state’

Driven by a highly precautionary regulatory environment and high financial investment from the state

Characterised by a combination of traditional companies and start-ups

Characterised by incremental innovations

Guided by restrictive regulations and standards

Supported by public funding

Steered by strong patent protection

How did we get here?

In this scenario, the synthetic biology value chain is driven by high financial investment from the state. This is because there are high regulatory burdens due to an uncertain outlook as to how the public and market environments will react to synthetic biology products. The state, therefore, needs to act as the main entrepreneurial force, while also incentivising the use of responsible synthetic biology through its funding streams. Companies that are already used to an intensive regulatory process (e.g. pharmaceuticals) will most likely adopt synthetic biology and integrate it into products or product development processes.

What are the opportunities?

- To have input into global risk evaluation strategies so that public funding could help companies move into new areas.
- A lot of competition could emerge, which would be good for the value chain (particularly those downstream). *‘This would allow us, in our business model where there are very few margins for cost, to get the best deals. I want to keep a pre-competitive, open-access state as much as possible.’* [1]

What are the risks?

- Not a very likely scenario in the US in future, but this is describing the trajectory synthetic biology is on now, but it may not be viable in the long run. *‘This scenario wouldn’t remain viable because we need to get to a world of resilience.’* [2]

Scenario 4: The sharing economy model

Summary table	
Main driving factors	Changes in industry structure through democratisation.
Configuration of value chain	Many small to medium size companies each providing specialised services.
Nature of innovative activity	Likelihood for disruptive innovations to emerge.
Nature of investments	Significant public funding into basic and translational research needed to allow the commercialisation sector to flourish.
Outputs of synthetic biology	Synthetic biology would be applicable to a wide variety of sectors.
Interplay between regulations and standards (types of standards)	Standards would include: • Behaviour and process standards to enable small companies to interact easily • Standards on what is patentable.
Nature of intellectual property	Strong clarity and robust protection of what is and isn't in the public domain. Standards describing what is and isn't eligible for an 'exclusive' patent and accessible licensing for research.

Scenario 4: The sharing economy model

Driven by changes in industry structure

How did we get here?

Big companies (in pharma, agritech, chemicals, etc.) have lost their position of power and instead there are many specialised smaller companies within the overall value chain. For example, there is one company for synthesis, one for design, one for PR, one for regulatory issues, etc. This allows individuals/companies to be able to take products to market more easily and with a lower start-up cost as they can pick and choose the parts of the pipeline (and the companies) that they need. *'This speaks a lot to me, but I would call it "ecosystem"…Companies all specialised on a specific part of the value chain and being the best at each area.'* [1]

What are the opportunities?

- While big companies dominate the sectors, the productivity and reputation of these big companies is decreasing, paving the way for smaller companies to emerge.
- Entering the era of genetic biotech means that many technologies (such as PCR) have come off patent, so this is a good time for development of technologies provided things are patented 'usefully' in the future. This would also mean IP offices could get better at narrowing the scope of patents appropriately.

What are the risks?

- There would be a push for a completely unregulated sector. *'We can't have open access to everybody, we still need containment.'* [2] This means that we would still need clear models for safety and efficacy testing.
- There is a necessary cost to innovation, social and economic, which needs to be recognised, and which may not be able to be borne by small companies alone. *'A world of permission-free innovation, or permission-based innovation, isn't right.'* [3]
- Moving from away from a situation where industries are dominated by big companies that have a lot of control, the IP landscape is very complex, and there are high regulatory burdens could be challenging and highly uncertain.

Steered by the sharing economy model

Dominated by lots of small to medium size companies

Characterised by disruptive innovations

Supported by public funding

Results in sector-wide applications

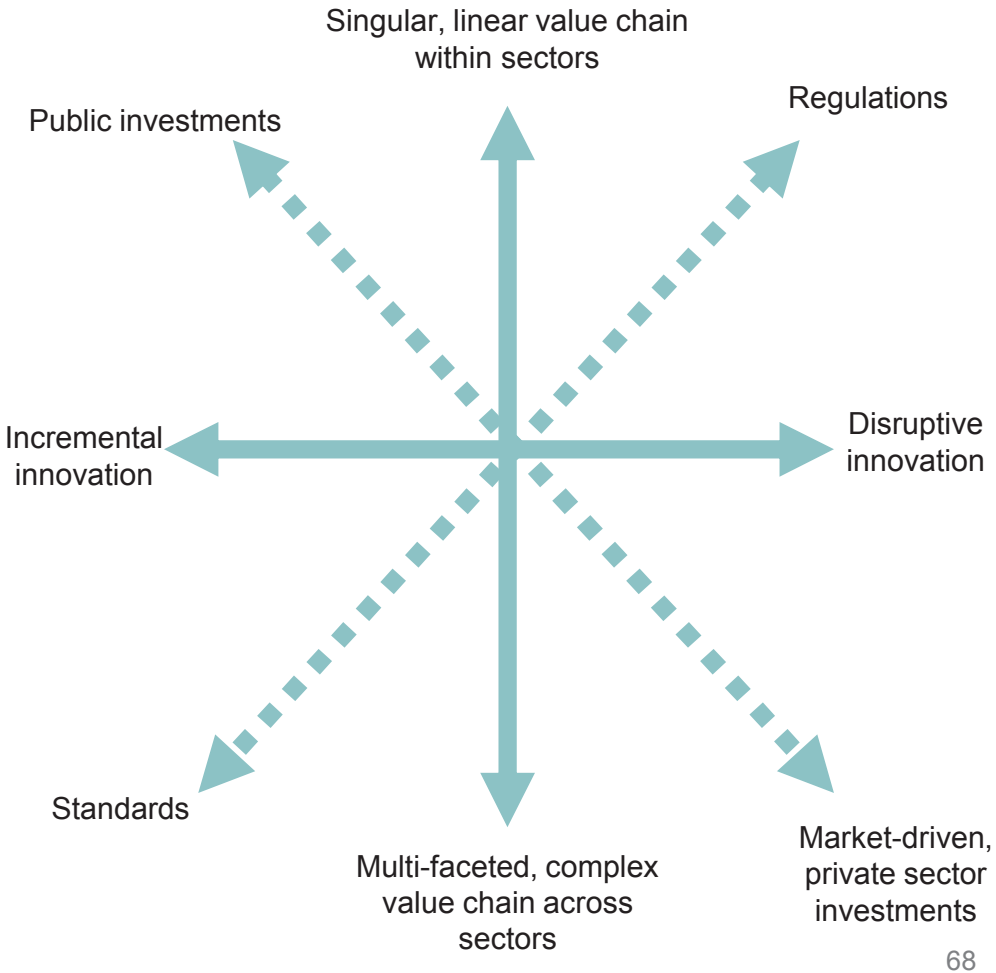
Learning from the scenarios

Drawing out lessons from scenarios is an iterative process. The aim is not necessarily to draw 'firm' conclusions, but rather to use the insights gained through the process to think about possible implications and lessons for the future. One way to think about this is through defining a set of axes and determining different trajectories the scenarios might take. These trajectories can be pushed in different directions by the drivers identified earlier and utilised through the scenario analysis. This is not a firm science, but for scenario analysis to be most useful, it can be helpful to play out a few different trajectories.

With this in mind, one possible future is where there are two outcome oriented axes (x and y-axes), over which we layer different drivers. For illustrative purposes here, we have chosen to highlight two of the axes that relate most closely to the original aim of the study, which was to identify the potential impacts of synthetic biology on the global marketplace.

Thus, we could ask:

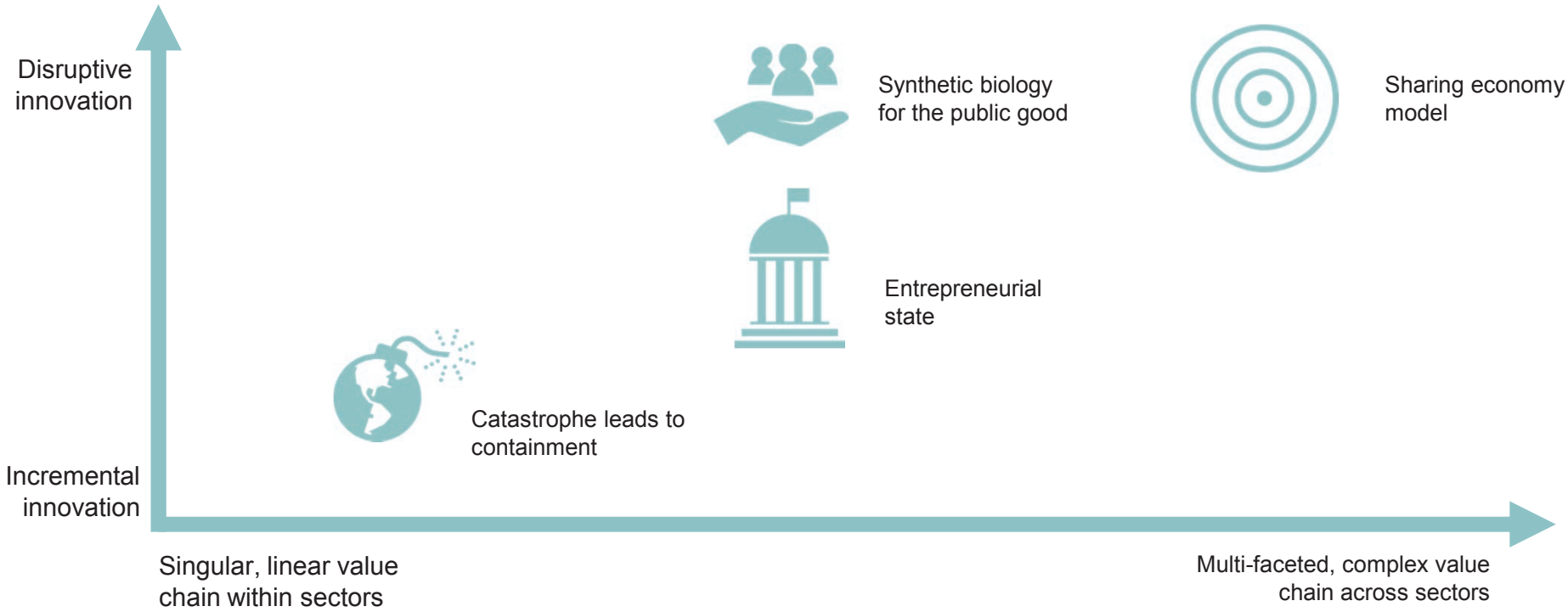
1. How do our scenarios map onto the main axes? Do they result in a more singular, linear value chain that primarily operates within single sectors, or do they result in more complex and multi-faceted value chains that can cut across sectors?
2. Do any of the scenarios favour incremental innovation vs more disruptive innovations?
3. What will be the effect of different drivers on the scenarios (e.g. standards vs regulations and public vs private investments)?



Lessons from the scenarios

Here, each of the scenarios is mapped onto the axes identified. In doing this mapping we do not intend to suggest one outcome (e.g. disruptive vs incremental innovation) is necessarily more favourable than another, but rather to illustrate how different outcomes from each of the scenarios are possible.

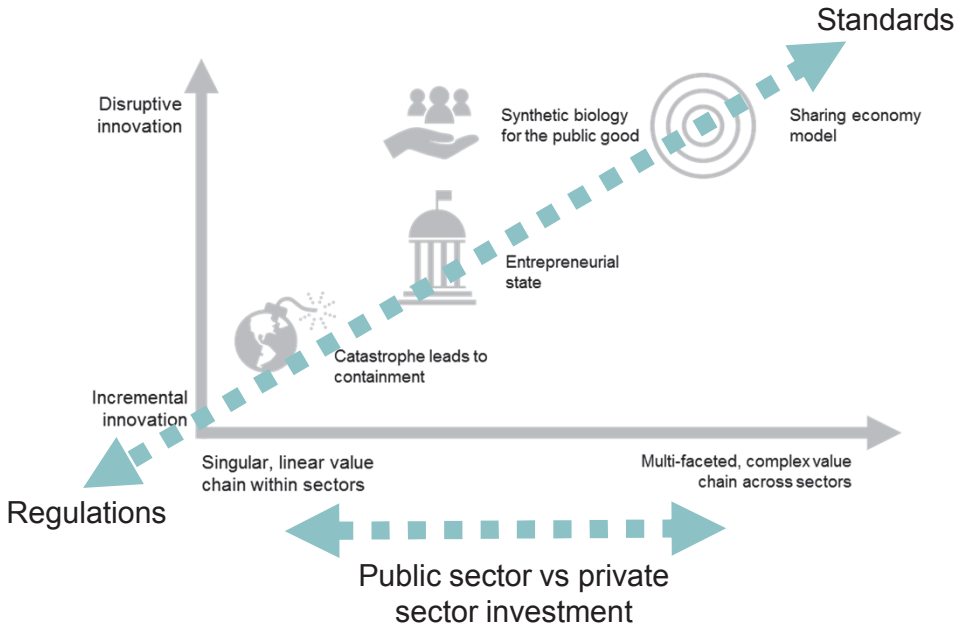
This kind of mapping allows us draw some conclusions about the way in which different drivers can affect the trajectories of the scenarios within the two main axes.



Learning from the scenarios

Standards versus regulation
If we think about the role that standards versus regulation might play within the scenarios, we can hypothesise that, generally speaking, standards might drive scenarios towards the top right corner. For example, the introduction of standards within the 'catastrophe leads to containment' scenario might help to unlock negative public opinion and may help to foster and facilitate integration across sectors by enabling a common vocabulary to be used. However, standards may not always have this effect. They could reinforce technological lock-in for companies where they were already dominant in a supply chain.

Regulations, on the other hand, might have an effect that drives scenarios towards the bottom left corner, characterised by incremental innovation within value chains. This might arise in a situation where synthetic biology needs to proceed cautiously and/or where a clear steer from government is needed to help signal to the market and spur investments.



Public sector versus private sector investments
Public sector and private sector investments can also have an effect on the scenarios. However, their effect may be much more dependent upon the existing location of the scenario. For example, large investments from the public sector in the 'catastrophe' scenario may help to accelerate disruptive innovations, but private sector investments might be more likely to be conservative due to the containment concerns. Thus, they might only maintain the scenario in its current position. Equally, public sector investments in the 'public good' scenario may help to expand the value chain if the private sector is nervous about returns. In short, what is perhaps more useful to focus on is the role that investments can play in helping to 'de-risk' emerging technologies by creating a lower risk envelope overall, though this is by no means guaranteed.

Cross-cutting insights from the scenarios

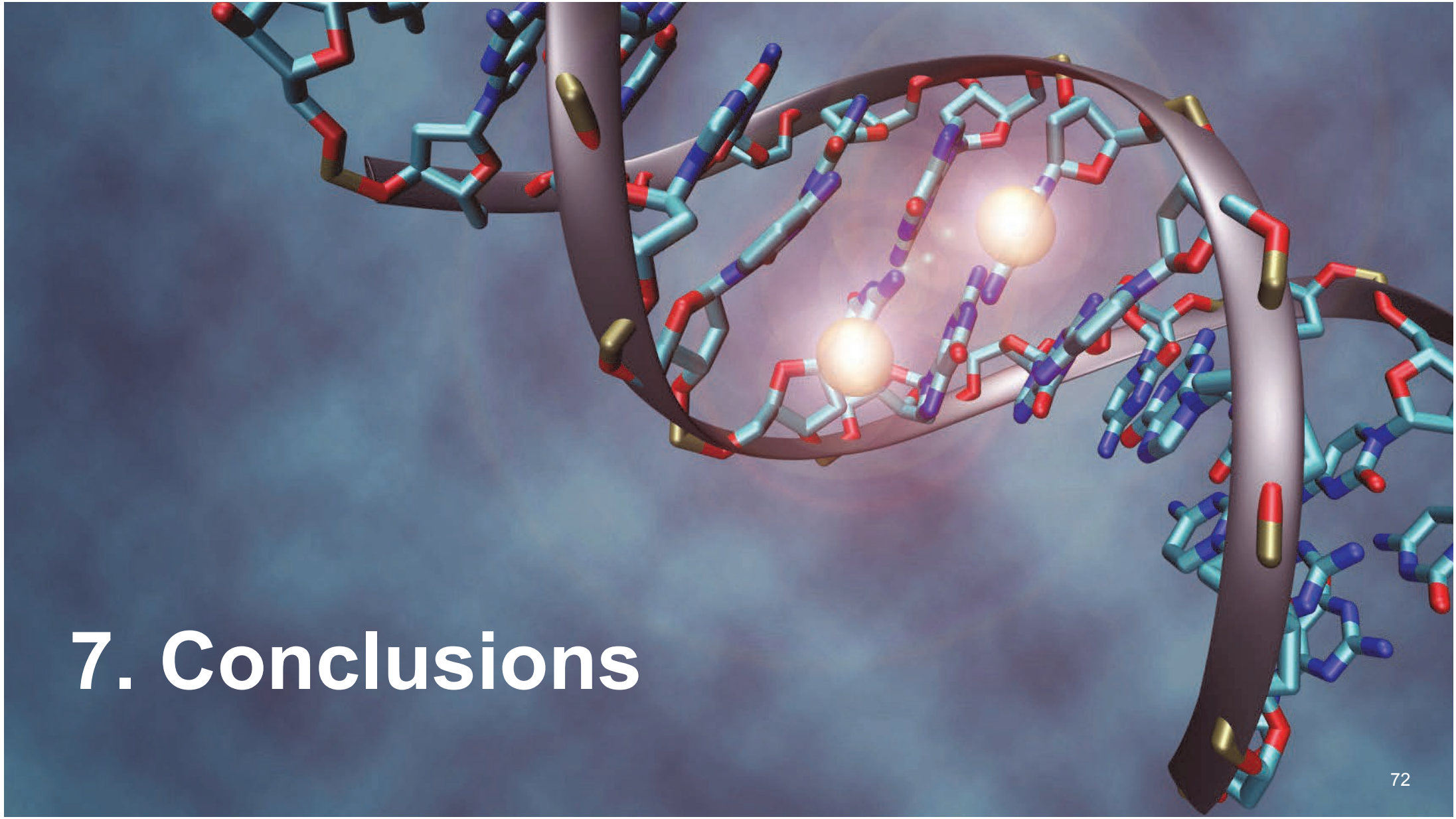
Catastrophe leads to containment

Synthetic biology for the public good

Entrepreneurial state

Sharing economy model

- Many of the PESTLE factors identified earlier could be classified according to whether they are ‘outcomes’ or drivers and a similar analysis to that done above conducted. However, it is important to recognise that not all of them have ‘good’ or ‘bad’ connotations. In the example given previously, incremental innovation may be desirable in some circumstances, such as with an emerging technology that has possible safety and/or public concerns.
- There are likely to be different weightings of the scenarios by sector; for example, the pharmaceutical sector is already heavily regulated and so is likely to stay engaged with developments in synthetic biology. This means scenarios with features like the ‘catastrophe leads to containment’ and the ‘entrepreneurial state’ may be more likely for this sector as the role of regulation will be a persistent feature in these sectors.
- It is worth noting that, in relation to thinking about the trade-offs between standards and other governance instruments like regulation, more regulation can have the effect of making things more expensive, which, in turn, could affect who can take part in the sector. This will affect the way the value chain looks and potentially makes disruptive innovation less likely because of the regulatory burdens.
- In any future, one will have to be mindful of the balance between different, juxtaposed drivers. For example, one will need to be careful that an abundance of regulatory activity isn’t matched by too many standards, and vice versa.



7. Conclusions

Conclusions

Outline of section

In this final section we highlight cross-cutting learning based on all sources of evidence and the scenario analysis. We then provide a series of recommendations and provocations for the future.

Overall, this report contains an array of issues relating to the nature of the synthetic biology value chain, the future evolution of the synthetic biology sector and the barriers, challenges and opportunities facing it. Standards can and should play an important role in this future; however, there will inevitably need to be a period of reflection and consideration on the ways to act.

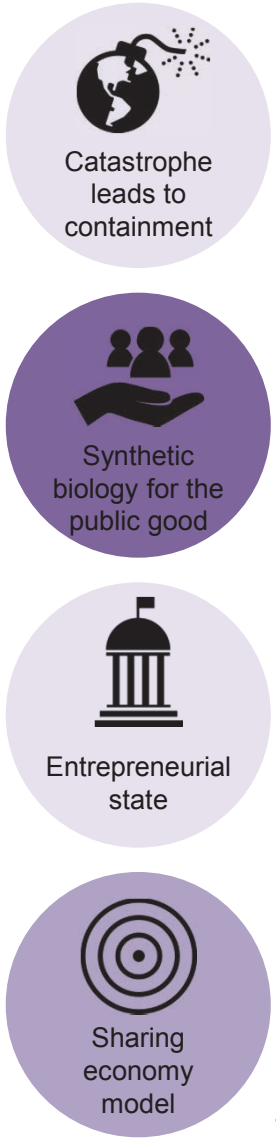
Learning from the scenarios and the value chain analysis – the idea stage

In the following four slides we integrate the findings from the scenario and value chain analysis by asking how standards could affect each stage of the value chain (idea, 'design-build-test' and scale up) within each of the four scenarios we developed (at right). We build on the barriers/challenges and benefits tables from earlier in the report and consider how the introduction of standards would or would not affect the scenarios.

At the idea stage, the introduction of standards could have implications for those scenarios where there is a dispersed value chain characterised by an array of small companies. This would be particularly strong in the scenarios where small companies play a defining role. Innovation and growth of the value chain in these scenarios is dependent on small companies coming up with ideas. Standards could help to ensure that these ideas are protected.

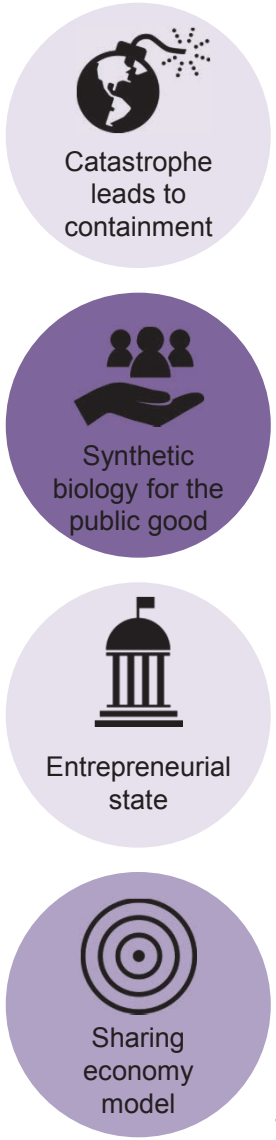
We expect that in scenarios that are highly regulated and where innovation is incremental and constrained within production processes, there would be very little impact of standards because there is little to no idea stage in the value chain. Even in a scenario where there is more space for innovation, any strong presence of the state implies less of a need for standards because there is already good central direction (a role standards might otherwise provide).

The strength of the effect of standard development at the idea stage on each scenario is summarised by the strength of shading (strong shades mean a greater effect of standards on the idea stage within the scenario).



Learning from the scenarios and the value chain analysis – the idea stage

	Barrier/Challenge	Potential benefits of standards
Idea stage	Reluctance of companies to consider synthetic biology at the idea stage due to scale up and regulatory hurdles.	Standards could help with production capacities as well as with simplifying the regulatory process.
	Reluctance of companies to change and adopt new techniques.	Standards could help people perceive synthetic biology as an interesting domain that is becoming more defined. However, this will require a cultural change and while standards will support the transition, they should not be expected to lead the change.
	Disconnect in understanding of industry needs by academia.	Standards could improve communication in the synthetic biology community and bridge different sectors.
	Poor exchange of information.	Classifying type of standards that will help build a common vocabulary.
	Not enough scientific advancements.	Technical standards could resolve some of the problems that currently take up resources.



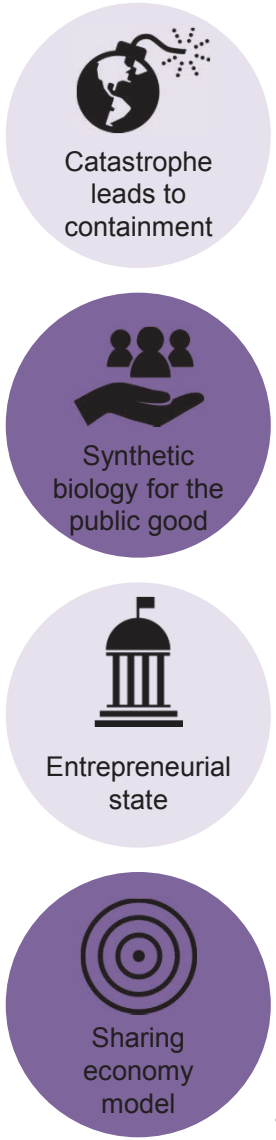
Learning from the scenarios and the value chain analysis – the ‘design-build-test’ stage

At the ‘design-build-test’ stage, the role of standards in promoting and enabling interoperability between companies will be important in order to facilitate the growth of a diverse range of companies that can add value at different stages of the value chain. Without interoperability, big companies will retain a hold on the value chain and competition will be limited. Thus, for those scenarios that project a role for a diverse range of smaller companies, the introduction of standards will be crucial (darker shading to the right).

Equally, standards will be important in the scenario that encourages development of the technology for the public good. This is because this scenario aims to foster diversification of companies and proliferation of new actors (and models of innovation, like public-private partnerships) within the value chain. Standards can help to coalesce these efforts in the absence of more direct state intervention.

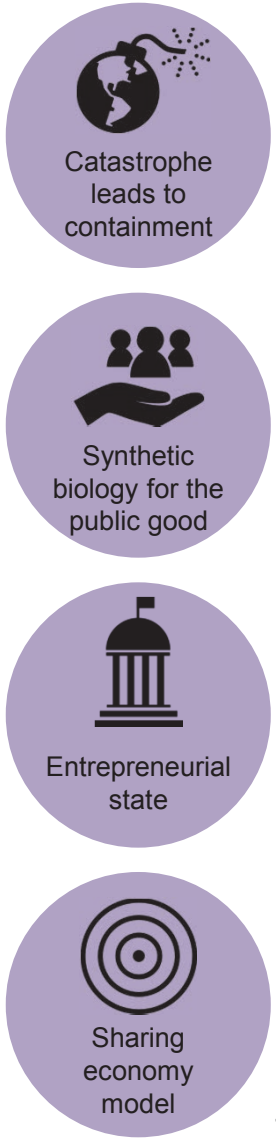
The strength of the effect of standard development at the ‘design-build-test’ stage on each scenario is summarised by the shading to the right (stronger shades mean a greater effect of standards on the ‘design-build-test’ stage within the scenario).

	Barrier/Challenge	Potential benefits of standards
Design-Build-Test	Lack of integration around equipment	Standards could help with the interoperability of the equipment and improve the workflow with providers and buyers.
	Lack of innovation around equipment	Standards can enable innovation by facilitating competition between and within technologies, therefore contributing to innovation-led growth.
	Intellectual property rights	Open standards can facilitate superior IPR for end-products.



Learning from the scenarios and the value chain analysis – the scale-up stage

Finally, at the scale-up stage, standards have the greatest potential to help overcome barriers and challenges and realise benefits of the value chain within each scenario. Standards that help to foster public trust would help across all scenarios as maintaining public trust will be key to evolution of the value chain within any future. For those scenarios that have a stronger role of regulation envisaged, standards could play an important role in simplifying the regulatory process across and between sectors for synthetic biology. Equally, for the scenarios where smaller companies play a larger role, standards could have an important role to play in helping to establish the market and facilitate future investments.



Learning from the scenarios and the value chain analysis – the scale-up stage

	Barrier/Challenge	Potential benefits of standards
Scale up	Lack of understanding of synthetic biology problems	Standards could facilitate understanding of the field by a person with less technical knowledge.
	Regulatory issues	Standards could simplify the documentation necessary for review by some competent authorities and reduce the review time associated with these processes.
	Necessity to scale up	Standards could allow reproducibility and reduce transaction costs therefore allowing greater productivity.
	Lack of a notable financial success	Standards have the potential to enable emergence of innovative products, which in turn could lead to financial successes.
	Need to attract investment	Standards could increase trust for private investors.
	Negative public perception	Standards could increase public trust. These type of standards could also be 'soft' standards like code of ethics.
	Environmental release concerns	Standards could help mitigate this risk by having clear containment requirements.

Learning from the scenarios and the value chain analysis – the process of developing standards

Finally, when it comes to the process of developing the standards, the following challenges and opportunities can be identified at each stage:

	Challenges and opportunities for standards development
Formulating standards	The scientific complexity of biology increases the difficulty of standardisation.
	Items or topics for standardisation must be chosen carefully in order to avoid stifling innovation by forcing technological lock-in. This is particularly the case in scenarios where disruptive innovation has a potential to have a large impact.
	Standards need to be specific so that they are widely understood and can be widely adopted. This will be important for interoperability in scenarios where there are multiple actors.
	Standards that are useful for industry may (or may not) be the same, or align with those that are useful for academics. There are few academic incentives for formulating standards as developing standards does not tend to lead to academic recognition such as publications or accessing research funding.
	Standards are more likely to be implemented if they are the result of a collaborative effort. This can be difficult to achieve, particularly with a global community. The larger the number of actors in any given scenario, the harder this becomes, but equally the more important a coordinating body (like BSI) becomes as a focal point for the discussions.
Adopting standards	It is harder to ensure adoption of standards than it is to formulate them. Ensuring standards add value encourages their adoption. In scenarios where there is a significant amount of public sector investment, it might be easier to adopt standards because the public bodies could make the adoption of standards a condition of funding.

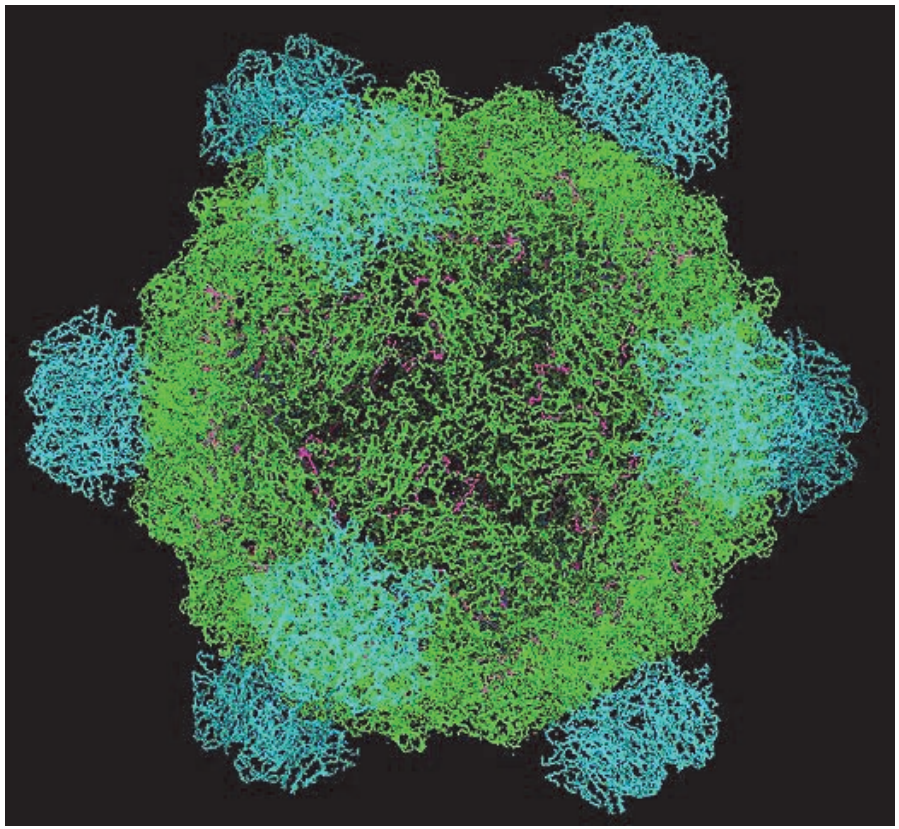
Learning from the scenarios and the value chain analysis – the process of developing standards

Finally, when it comes to the process of developing the standards, the following challenges and opportunities can be identified at each stage:

	Challenges and opportunities for standards development
Long-term impact	The timing of standards is important. Premature standardisation could lead to stifling of innovation, whereas late standardisation could risk missed opportunities. Implications of timing are quite important for the different scenarios. Where you don't have much government involvement, standards might stifle innovation before it gets going.
	Due to the nature of synthetic biology, standards chosen now may have only a brief utility. This could deter individuals from engaging in standard setting.
	The degree of impact that standards bring is dependent on the position the activity has in the value chain. Some companies' activities could be rendered obsolete by the introduction of standards.
	Standards could give weight to the field by contributing to it being perceived not only as an interesting domain but one that is becoming more and more defined. However, this will require a cultural change and while standards will support the transition, they should not be expected to lead the change.

Recommended areas for action

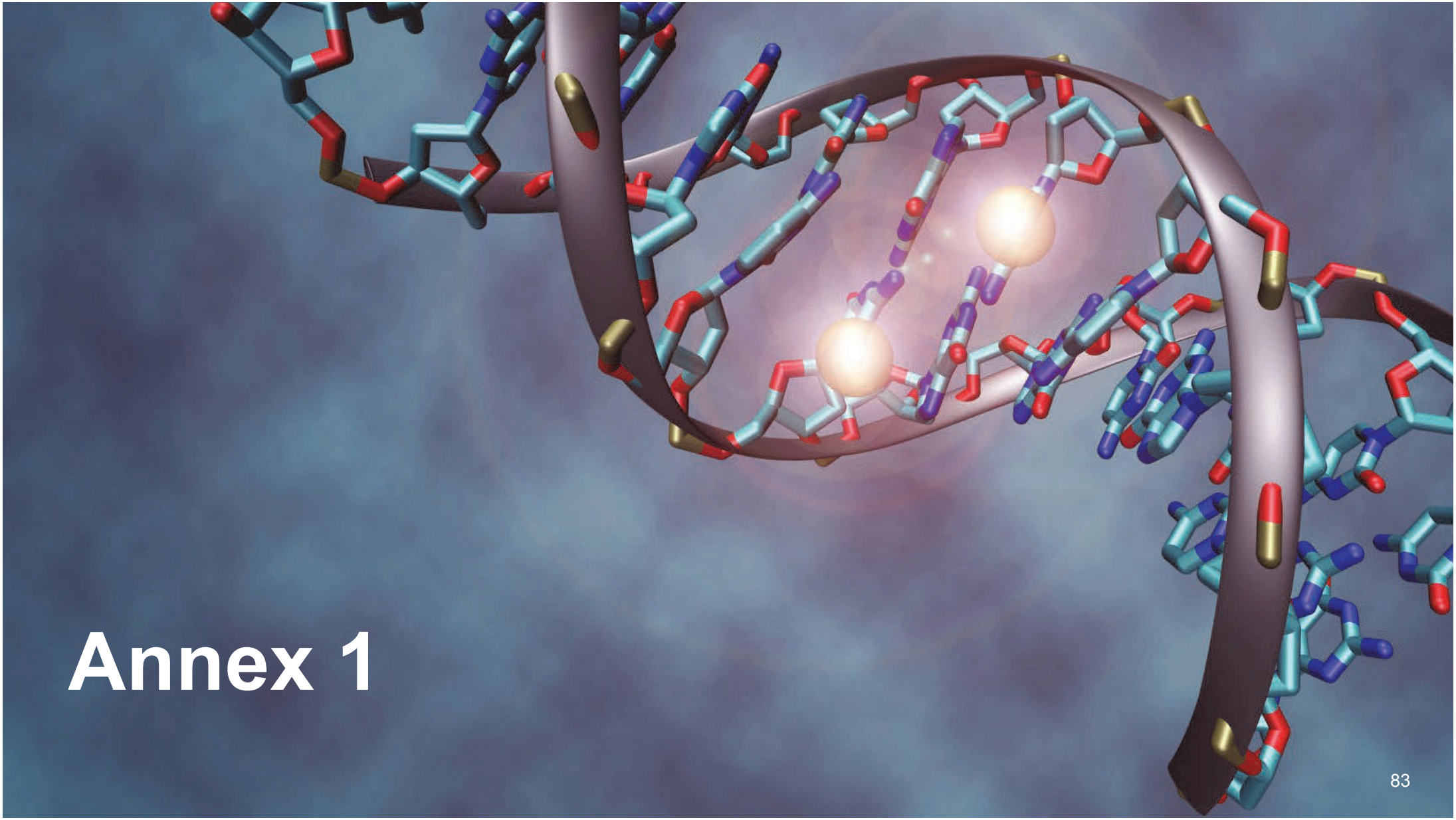
- **Address public trust and confidence in the future market.** Public trust and confidence is a major distinguishing feature of synthetic biology from other emerging technologies. As one interviewee pointed out, ‘the biology industry isn’t that different to the chemical industry, it’s just that with biology, people fear it might take over the world’. Maintaining public trust through various governance instruments, including standards, will be paramount. An important consideration is how standards can reflect and be seen to reflect concerns of a spectrum of stakeholders.
- **Utilise standards to identify key benefits for end users.** Related, a key challenge for the value chain at the moment is to make clear to end-users what the benefits of synthetic biology are, particularly when the end-user is the general public. An overriding feeling from the interviews was that the key to public acceptability is to make the benefits of synthetic biology very clear to consumers, while acknowledging the risks.
- **Standards could contribute to synthetic biology being perceived not only as an interesting domain, but one that is becoming more defined.** However, this will require a cultural change and while standards will support the transition, they should not be expected to lead the change.



Provocations for the future

The final set of points below raise a series of issues, in the form of provocations and questions for the future, which are worth considering on the basis of our analysis.

- **The analysis of the value chain presented here is novel and could be used to frame discussions for the sector.** It will be interesting and important to consider the framework for the different stages of the value chain presented here and the ways in which synthetic biology feeds into other sectors – through absorption and selling-in. Monitoring this as the sector grows will be an important area of ongoing research, which could help to structure priorities for future standard development.
- **Does it matter who sets the standards?** The role of BSI might be very different in each of our scenarios, or in any future scenario that plays out in the real world. For example, in a scenario based on the sharing economy, BSI might play a facilitation role. In the scenario based on containment, BSI may need to work most closely with the state and larger companies to help manage public trust, while in the scenario about the public good, BSI might have to help coordinate actions within the value chain to maintain public trust. These roles may also change as the sector develops and the value chain changes.
- **What should the role of public-private relationships be and how can they help to overcome market and institutional failure?** Standards could play a role in identifying and supporting areas for public-private relationships to maximise the potential of synthetic biology and overcome market and institutional failures. However, this will need to be monitored closely as sectors bring the benefits of synthetic biology closer to the market.
- **What future scenario would BSI and its stakeholders like to see realised and what elements from the four scenarios here could help that?** Is a diverse value chain with many small companies desirable? Is a highly entrepreneurial state needed now, but with a view to helping move towards a more market-driven scenario in future? Working with stakeholders to determine elements of future scenarios that are desirable will be important to understanding and determining shaping actions that can be taken today.
- **Due to the enabling role synthetic biology can play, there may be a need to look at how standards intersect with other industrial ecosystems.** As synthetic biology often enables other industries, it is possible that in some industries the development of standards that could push this field forward might be countered by some players due to market forces. The success of standards should be judged taking into account the ecosystem of each industry.



Annex 1

Interview selection and distribution of participants

The selection of the interviewees began with compiling a database with companies' names that are using synthetic biology. The strategy for compiling this database was the following:

1. Collate company names from two databases: Synbioproject (http://www.synbioproject.org/cpi/application) and Synbiobeta (http://synbiobeta.com/company/).
2. From the documents selected during the literature review, extract relevant names of persons working in synthetic biology – either in companies or academia.
3. Ask for recommendations on relevant companies and persons to contact from the interviewees as the interviews progressed.

The database compiled contained over 200 companies.

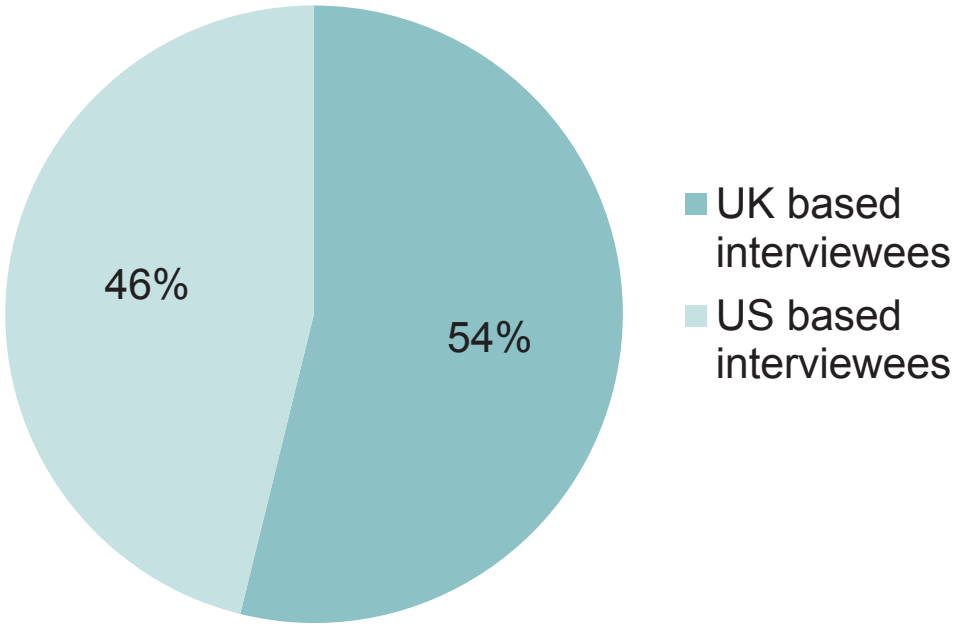
As the database was being compiled, invitations for interviews were sent to companies that met as many of the following criteria as possible: (1) had synthetic biology products that were marketed or close to market; (2) were mentioned in the scientific literature as companies that engaged in synthetic biology; (3) were big companies from established industries that at one point engaged with synthetic biology companies; (4) were academics that published research in this field.

The total amount of interviews conducted for this projects was: (i) 26 for the first round of interviews and (ii) 7 for the interviews exploring the scenarios.

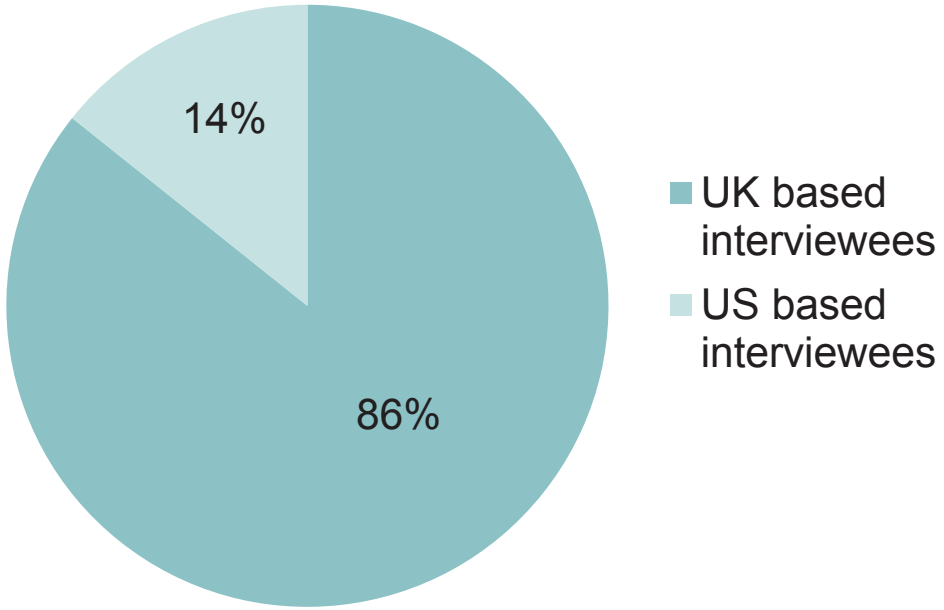
The following slides present the distribution according to the interviewees' geographical location and position in the value chain. While an interviewee can be a company that has activities in several sectors in the value chain, for the purpose of easier tracking, the companies were placed in just one segment – the one they mostly focus their activity in.

Interview selection and distribution of participants

Geographical distribution of participants in the first round of interviews (n=26)

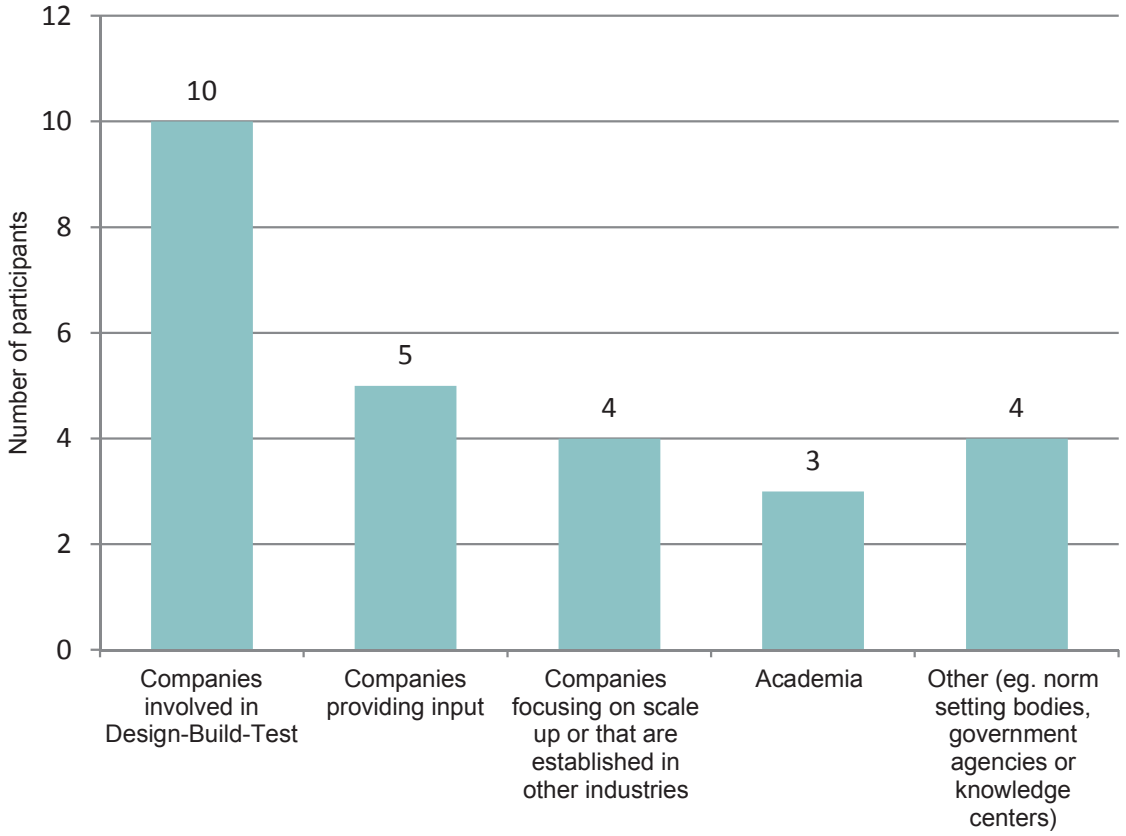


Geographical distribution of participants in the scenarios interviews (n=7)

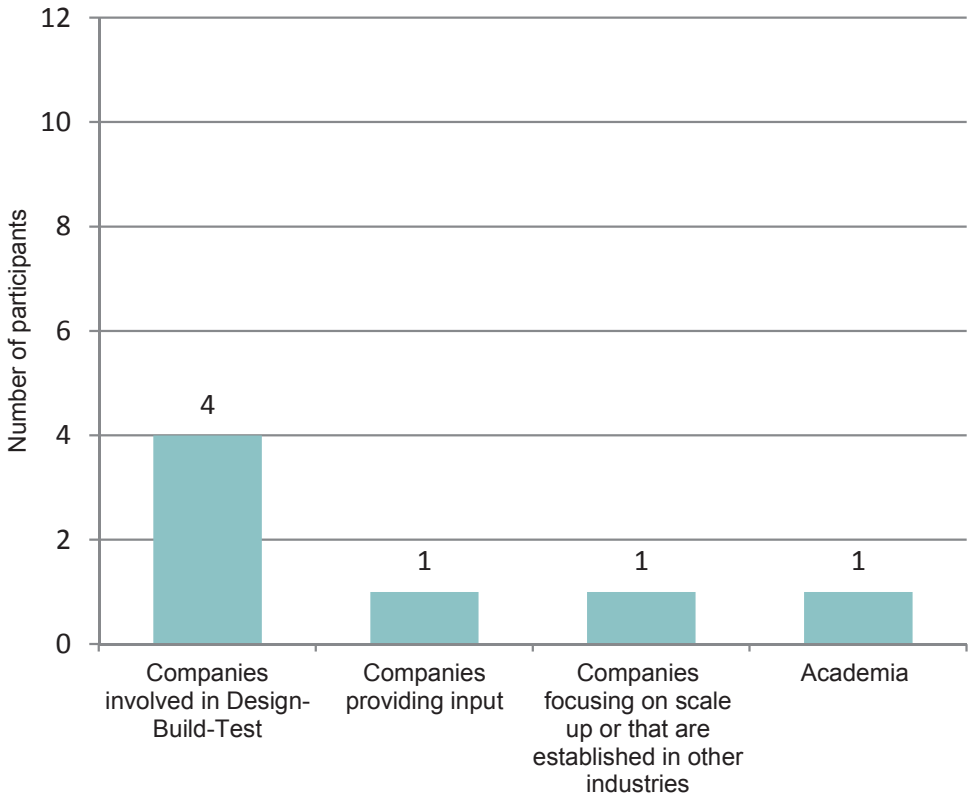


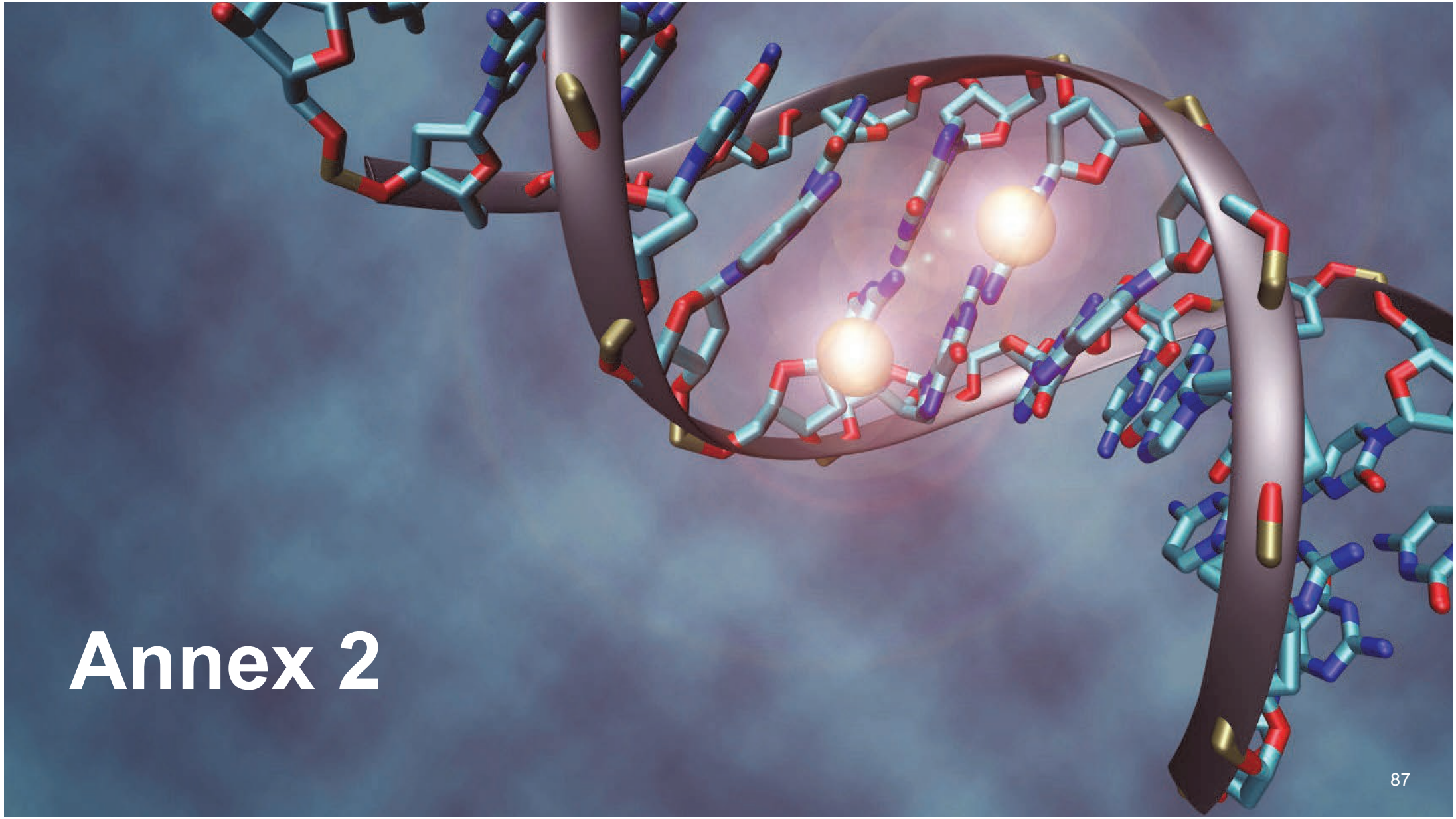
Interview selection and distribution of participants

Distribution of participants in the first round of interviews according to their activities' position in the value chain



Distribution of participants in the scenarios interviews according to their activities' position in the value chain





Annex 2

Semi-structured interview protocol

General background

Could you please tell me a bit about your job and role and how this relates to synthetic biology?

Related to the previous question, what is your own disciplinary background and how did you come to work in your present role?

How would you define synthetic biology?

What do you think makes it distinct from other branches of biology? [e.g. genetic engineering]

Are there specific areas of synthetic biology where the UK *(or US as relevant to the interview)* has a global competitive edge? If so, what would those areas be? Do you see this changing over the next five year period?

The value chain and your company

As part of this work we are exploring the synthetic biology value chain within and across sectors. By value chain we mean a way of thinking about the different elements that can be used to describe a company's business activities and how each of those elements adds value in the production of products and services. As synthetic biology may be described as an enabling technology to a wide variety of industries, rather than an industry in itself, this is not straightforward as there may be many value chains, rather than just one. To help us think about this and construct a value chain we will now ask some questions about your company.

Does your company fit into a particular industry/ies? If so, which one(s)?

Could you give us some examples of your synthetic biology R&D, services or products?

Who do you sell or market your services/products to? Is this the same as the ultimate 'end user'?

Who would you like to sell/market to in future? Do you market across sectors? Nationally and/or globally?

Who are your 'suppliers'? Do your suppliers cross sectors? National/international borders?

Do you carry out internal R&D or do you sub-contract this expertise?

Given all of the above, how would you summarise the business model of your company for synthetic biology?

Semi-structured interview protocol

The future, barriers and opportunities

We'd like to ask you some questions now about your perceptions of the future of synthetic biology and any future barriers and opportunities.

In your opinion, is synthetic biology likely to result in brand new products such as alternative therapeutics/medical/industrial applications?

Do you think commercial applications of synthetic biology are more likely to improve/speed up existing production processes?

How much more efficient and effective will these applications make things? Over what timescales?

Can you give some examples of the types of applications that will make this more efficient/effective?

Standardisation

We're going to ask some questions now about the potential role of standards in relation to the barriers and opportunities we just discussed. A standard is a document that defines best practice, and is established through consensus. Standards set out clear and unambiguous provisions and objectives so they can help to facilitate common working practices/relationships across a sector. The point of a standard is to provide a basis for businesses, academia and consumers to share the same expectations about a process, method, product or service. Standards can act as an enabler for innovation to take and help bring new technologies, product, services and concepts to market more quickly and safely.

What is your understanding of a standard?

What are some of the barriers your company faces in relation to the wider synthetic biology environment?

Are there particular barriers in relation to end users for your company adopting synthetic biology products? Are there different barriers you see for the sector as a whole?

What are some of the main opportunities you see for your company in relation to the wider synthetic biology environment?

What needs to happen in order for your company to realise these opportunities? *(e.g. more money, research breakthrough, changed legal frameworks, changes downstream/upstream in the value chain, etc.).* For the sector?

Semi-structured interview protocol

Standardisation (continued)

Do you think the barriers/opportunities you just described differ from those affecting: Companies who you buy products from? Companies who you sell products to?

Do you think there are areas where standards could help your company in any of the following ways, and if so, how?

- Allow you to maximise market opportunities or enter new markets? Work more effectively with either providers or buyers?
- Enable more (or more efficient) innovation/technology development within your company or the field? Develop more applications for synthetic biology?
- Enable a shared understanding with anyone in the value chain or end users? Support production processes?

Are there areas where standards would hinder any of your company's activities?

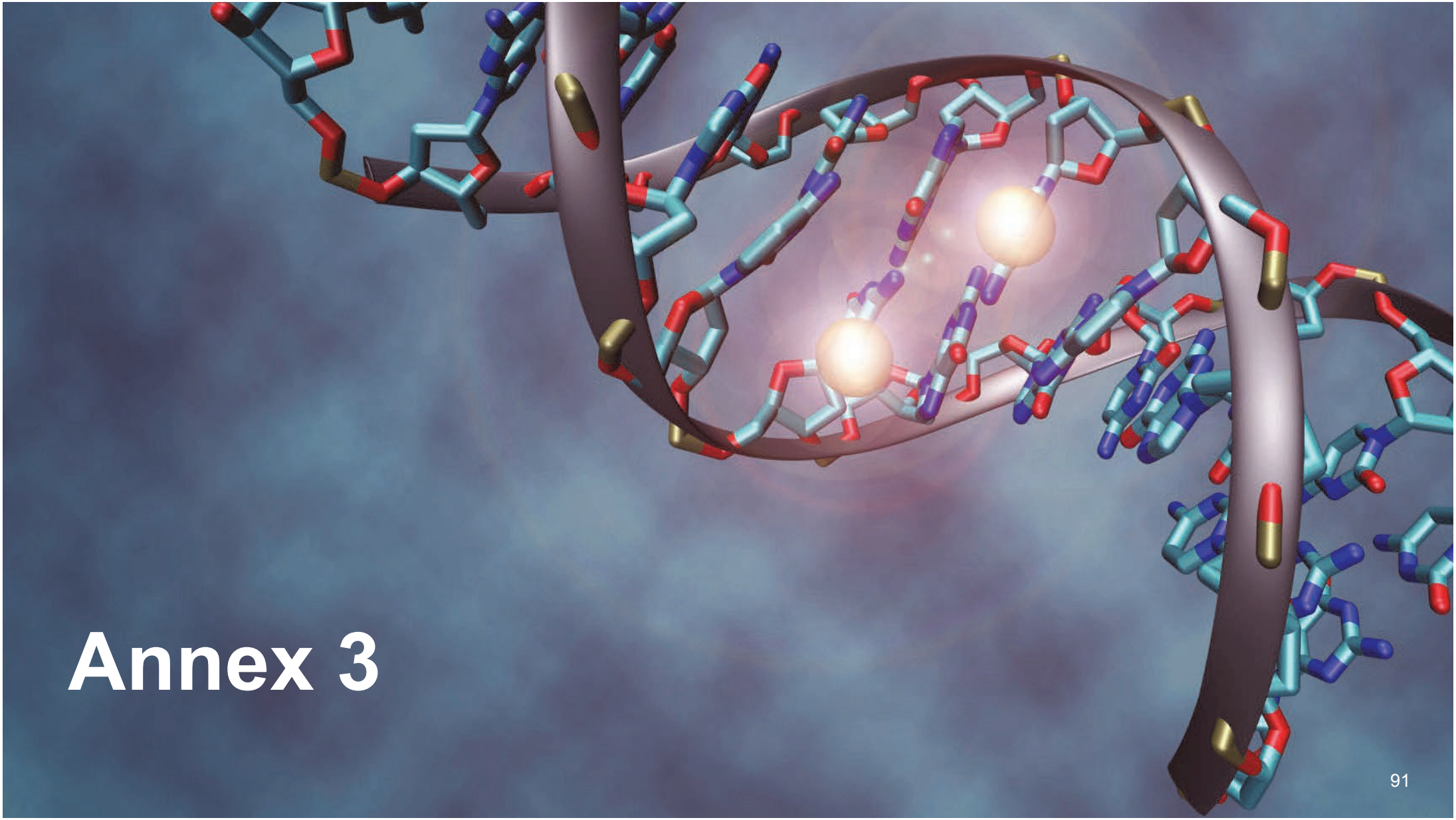
How might standards help synthetic biology players overcome some of the challenges they are currently encountering? What areas of standard development in particular are important?

In relation to the standards that you mentioned, what do you foresee as the barriers and challenges in adopting them for your company?

Concluding

Are you aware of any efforts to explore the potential for standards in this field? Do you think there is a need to work together across the field to develop an approach to standards?

Is there anything else you would like to add about your experience of working in synthetic biology and how you feel about the potential role of guidelines/codes of practice in this field?



Annex 3

Rapid evidence assessment

- We conducted a rapid evidence assessment in order to provide an overview of the available literature on the synthetic biology industry and value chain and understand the various factors associated with its development.
- A number of strings of search terms were developed for each category. The complete list of search terms is provided in Table 1.
- The search was conducted using Pubmed, EBSCOhost, Google Scholar and a standard Google search in order to ensure coverage of the full range of academic, policy and consultancy literature. The first 50 results of each search (with results ordered by relevance) were screened and relevant documents extracted. No restrictions were placed on date of publication.
- Additionally the rapid evidence assessment relied on official or non-official documents provided by the British Standards Institute (BSI).
- A total of 53 documents were reviewed. The most relevant ones were entirely read whereas for secondary ones, keywords were used to extract relevant data and then screened entirely if necessary. Details of keywords are provided in Table 1.

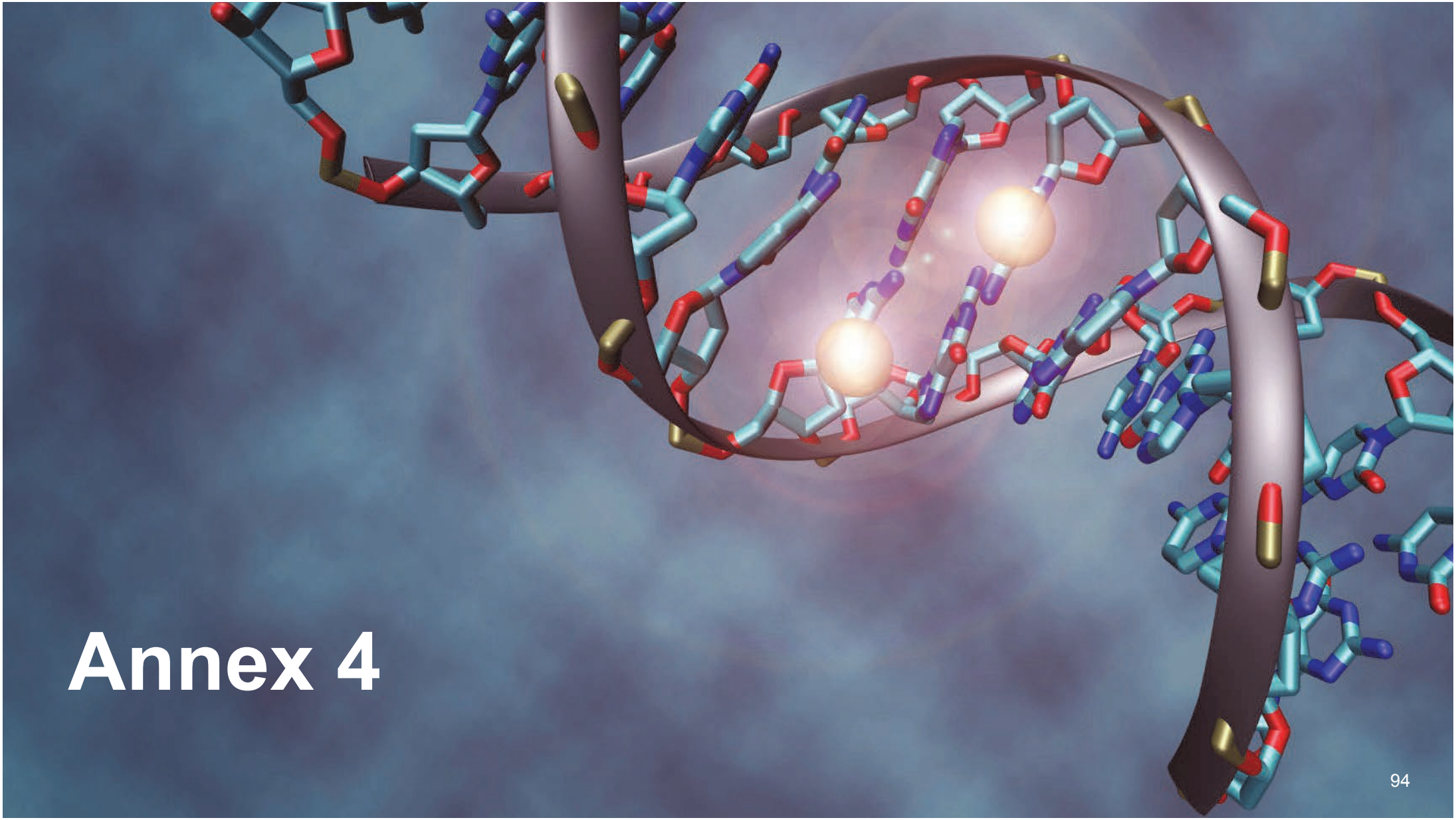
Table 1. List of search terms used in the rapid evidence assessment

Category of literature	Search terms	Keywords
Literature on synthetic biology in relation to PESTLE factors and standards	“Synthetic biology” “synthetic biology standard*” “Synthetic biology ethic*” “Synthetic biology regulat*” “Synthetic biology govern*” “Synthetic biology business OR economy”	Politic*, govern*, internat*, cooperat*; Econom*, business, financ*, Invest*; social, public, society, ethic*, acceptability, perception; technic*, technolog*, process, scienti*, complex*; legal, law, regulat*, risk* standard*, “intellectual property”, patent*, justice; environment*, ecosystem*, eco-system*

Rapid evidence assessment

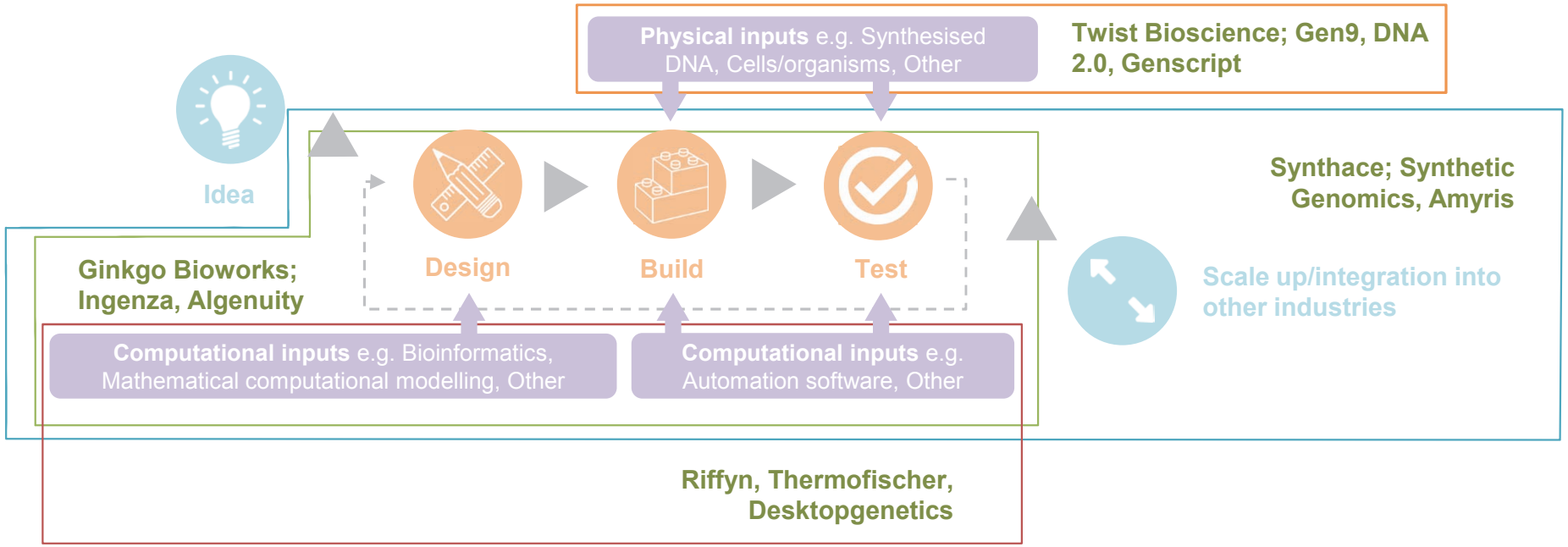
Table 1. List of search terms used in the rapid evidence assessment (continued)

Category of literature	Search terms	Keywords
Literature on value chains	“value chains”; “global value chains”; “value systems”; “business models”; “synthetic biology” AND “value chains” OR “global value chains” OR “value systems” OR “business models” Biology AND “value chains” OR “global value chains” OR “value systems” OR “business models” DNA AND “value chains” OR “global value chains” OR “value systems” OR “business models” “biotechnology” AND “value chains” OR “global value chains” OR “value systems” OR “business models” genetics AND “value chains” OR “global value chains” OR “value systems” OR “business models” genetic engineering AND “value chains” OR “global value chains” OR “value systems” OR “business models” Gene AND “value chains” OR “global value chains” OR “value systems” OR “business models” Knowledge AND “value chains” OR “global value chains” OR “value systems” OR “business models” Innovation AND “value chains” OR “global value chains” OR “value systems” OR “business models” Invention AND “value chains” OR “global value chains” OR “value systems” OR “business models” Technology AND “value chains” OR “global value chains” OR “value systems” OR “business models”	

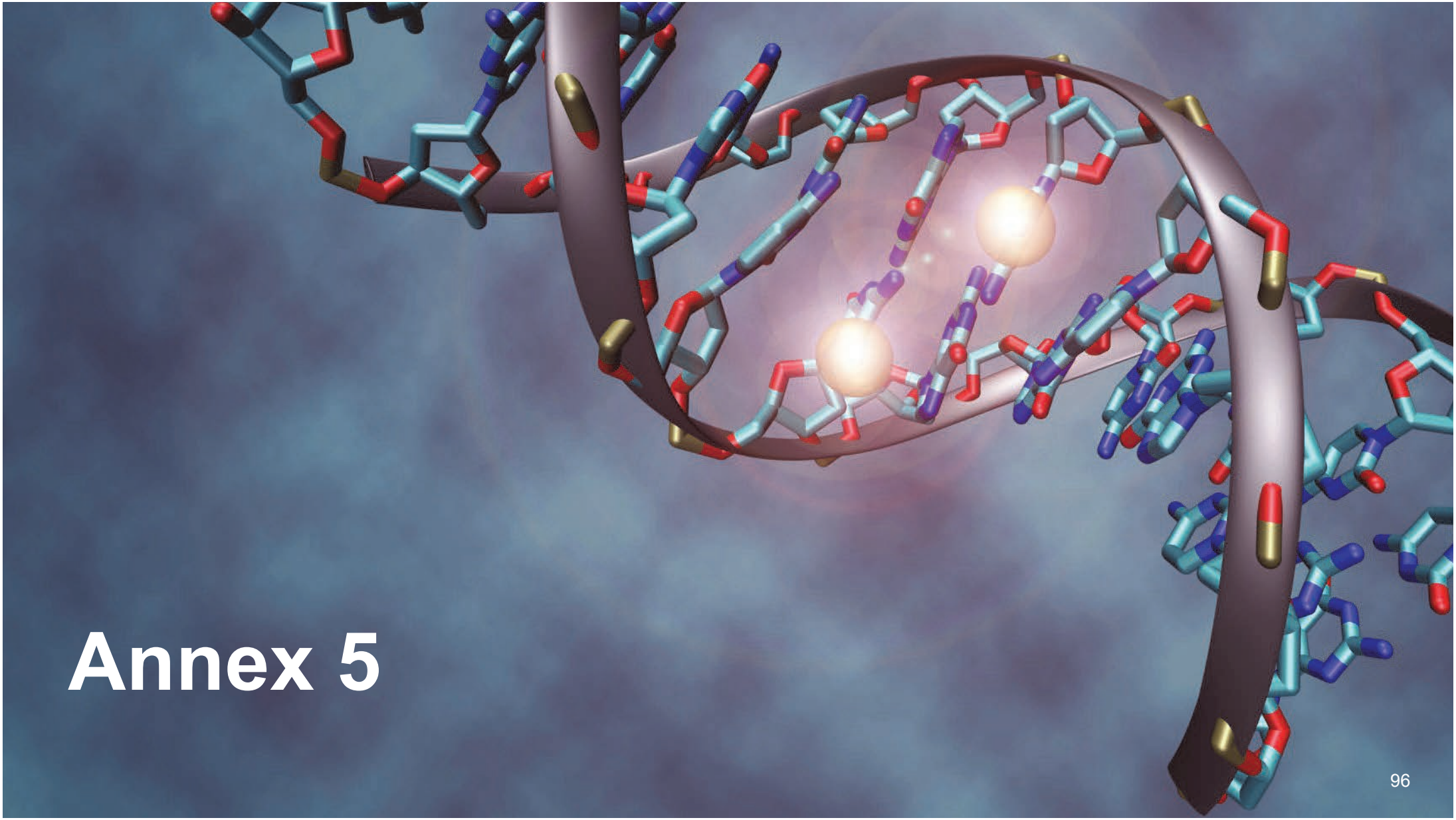


Annex 4

Examples of companies mapped onto the value chain



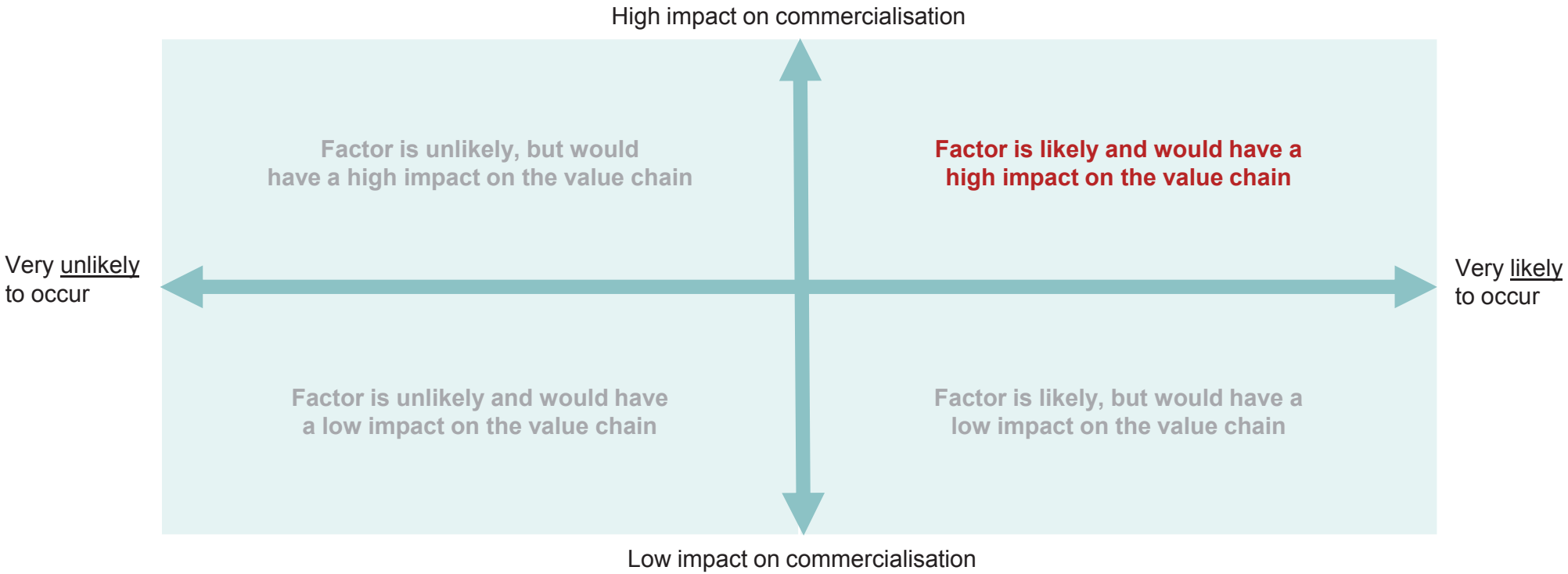
Note: This identification and mapping is the analysis of the research team, not a self-identification of the companies themselves.



Annex 5

Mapping of PESTLE factors to inform the scenario analysis

In order to identify the PESTLE factors used to build the scenarios, we prioritised the factors using the matrices presented below. The subset was determined on the basis of which factors were likely to have a high impact on commercialisation and very likely to occur (first set of matrices), as well as having those that standards were likely to be able to influence (second set of matrices).



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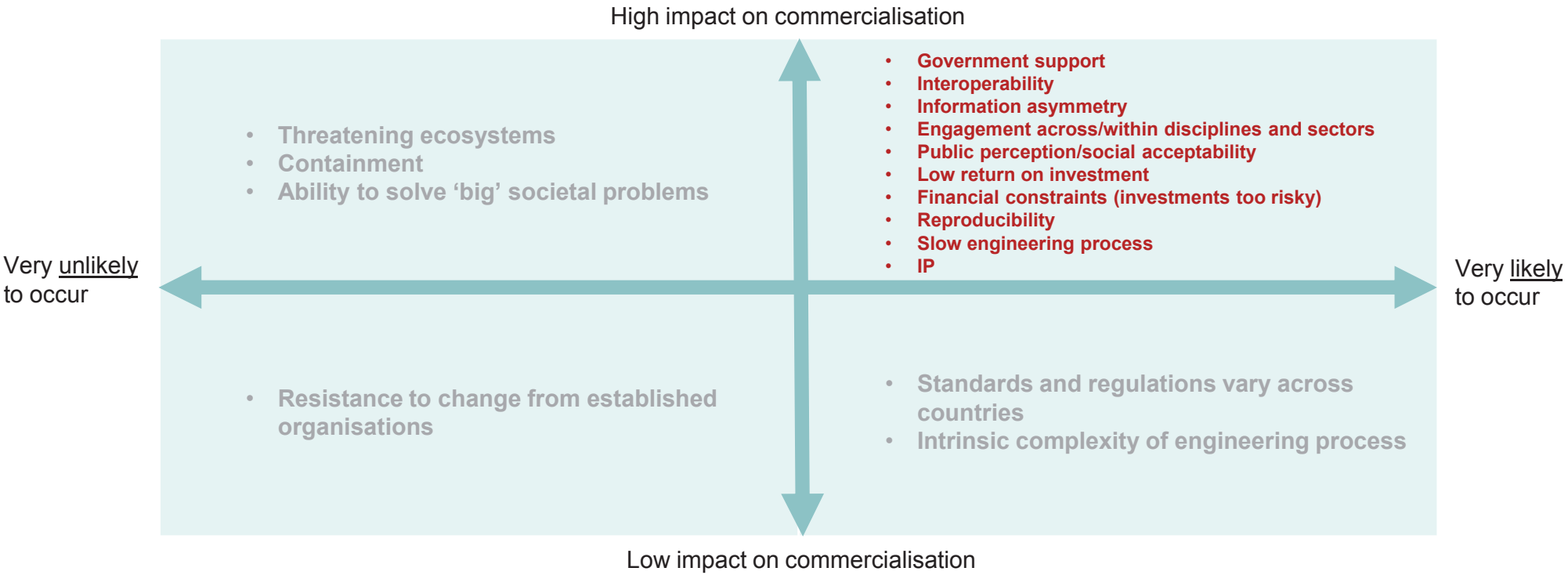

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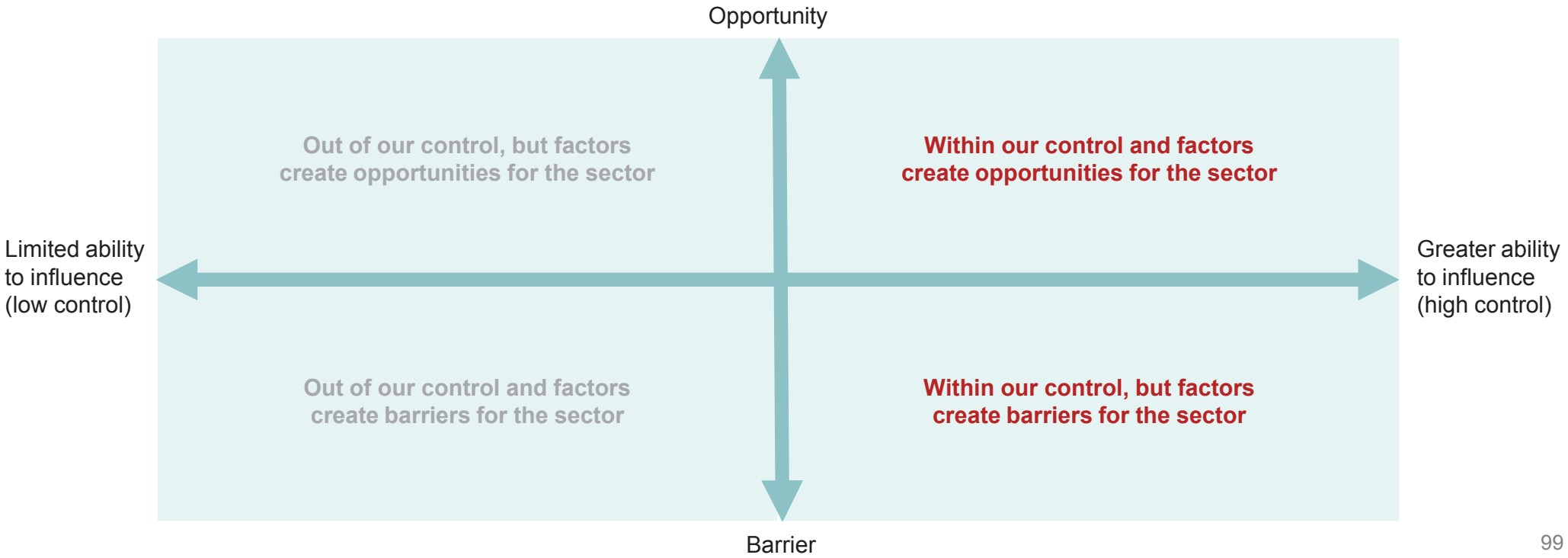
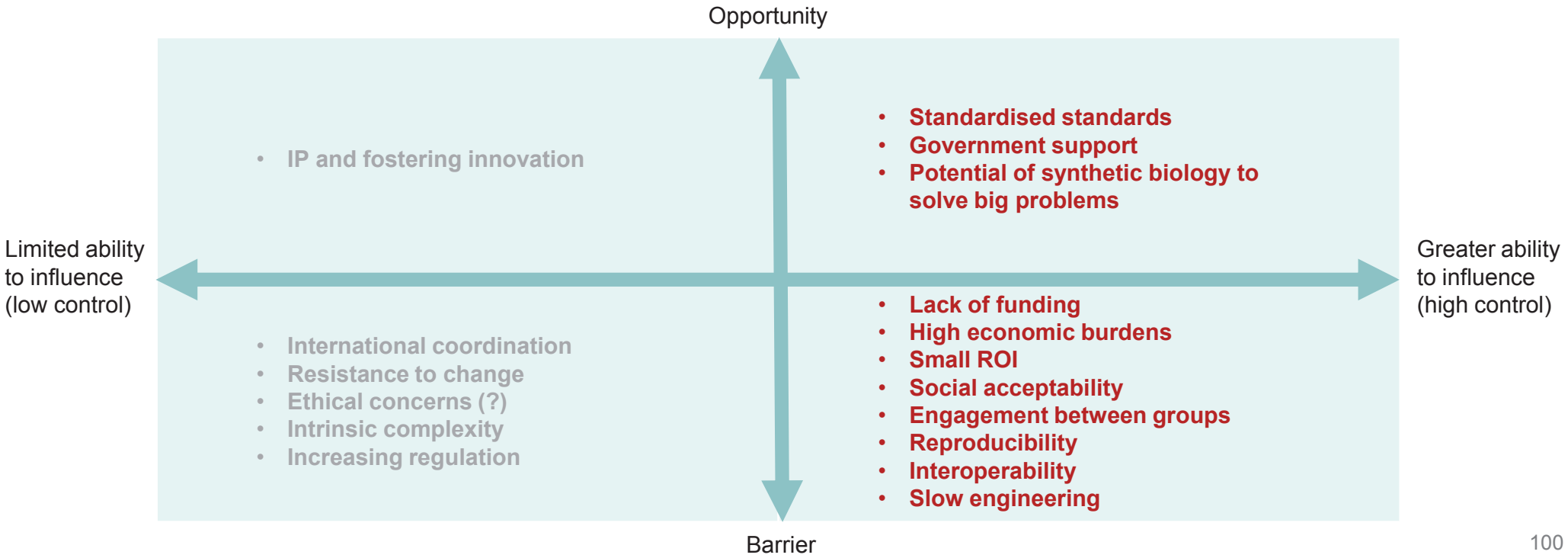


Mapping of PESTLE factors to inform the scenario analysis

In order to identify the PESTLE factors used to build the scenarios, we prioritised the factors using the matrices presented below. The subset was determined on the basis of which factors were likely to have a high impact on commercialisation and very likely to occur (first set of matrices), as well as having those that standards were likely to be able to influence (second set of matrices).



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[1] Scenario interviewee 4.

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[1] Scenario interviewee 2.

[2] Scenario interviewee 6.

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[1] Scenario interviewee 5.

[2] Scenario interviewee 2.

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