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Executive summary

- Technological solutions in engineering biology, both those that are emerging now and those that have the potential to emerge in the future, could help solve the most pressing issues faced by society - ranging from new fuels which could support Net Zero ambitions, to the delivery of personalised cancer medicines. However, realising these ambitions will rely on the UK's ability to manufacture solutions at scale, and there is not currently sufficient support for research or translational activities to enable this to happen. To change this, and enable the scale up of engineering biology-based solutions, there must be better coordination of investment across the landscape, including into technology readiness levels.

- Current supply of skilled workers for engineering biology is not sufficient to meet the forecasted demand to deliver solutions at scale and this could hold back the economic benefits and potential that engineering biology could otherwise drive.

- Emerging engineering biology solutions that crossover with different areas of knowledge, such as Artificial Intelligence, do not currently align within existing regulatory limits and have associated security risks. There is a need to develop more advanced safety checks, which don't stifle innovation, and consider innovative approaches to regulation by aligning work from multiple regulatory bodies.

- The UK must have a constant and adequate supply of sustainable biomass feedstocks that can be used to manufacture bioproducts via engineering biology approaches. In particular, optimised seaweed biorefineries will economically strengthen the UK's manufacturing industry and circular bioeconomy, and help the UK to achieve net-zero status. However, feedstock production yield data is currently difficult to obtain, pre-existing feedstock technologies may not be compatible with 'new' feedstocks such as seaweeds, and there is work to do to build public support for these types of applications.

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This response was coordinated by Luís Miguel Lacerda, policy adviser in the Policy Impact Unit, UCL STEaPP. As active members of the community, we wish to help the committee support appropriate guidance to fullfill the ambitions of the National Vision for Engineering Biology.

What are the key applications for engineering biology?

1- Some of the key applications for engineering biology are:

(i) **Sustainability**, for example finding new routes to produce fuels and chemicals to reduce the reliance on fossil fuels or by capturing carbon to reduce the impact of greenhouse gas emissions;
(ii) **Cellular agriculture**, which creates meat replacements based on plant proteins in bioreactors rather than from farm animals;
(iii) **Health**, for example through personalised medicines such as viral vectors gene therapies, vaccines or gene-editing techniques like CRISPR. Other health applications include CAR-T cell therapies - a type of personalised immunotherapy which introduces genetically-modified immune cells into a patient's body that are programmed to recognise and kill cancerous cells. This activity can include manufacturing autologous (using immune cells from the patient) CAR-T therapies at the bedside or in automated "GMP-in-a box" system[1], which can deliver cost reductions, accelerate bench-to-bedside innovation, and mitigate risks that are generated by market shortages[2] in supply chains. While Engineering biology can lead to these new therapeutic products, it can also lead to improved bio-based tools used in their manufacture, leading to lower costs.

How can Government policy support the development of engineering biology?

1- Whilst there has been substantial government investment made in the past on synthetic biology (BBSRC Synthetic Biology Research Centres (SBRCs)), there is currently not enough groundwork to support the scale up of engineering biology-based solutions and business. This is in line with recent advice from the Council for Science and Technology on Engineering Biology which recommends that Government "should work with industry and UKRI to establish multidisciplinary Biomanufacturing Innovation Centres, for testing, scale up, and commercialisation of non-health engineering biology applications, including materials and fuels"[3]. This advice speaks to

[1] Pereira Chilima, T. & S. Farid. 2019. 'A roadmap to successful commercialization of autologous CAR T-cell products with centralized and bedside manufacture.' Cell Gene Therapies VI 73. Comisel, R. 2022. Decisional Tools for Supply Chain Economics of Cell and Gene Therapy Products. Diss. UCL (University College London).
[2] Bicudo, E. & I. Brass. 2023, 'Advanced therapies, hospital exemptions & marketing authorizations: the UK's emerging regulatory framework for point-of-care manufacture' Cell and Gene Therapy Insights 9(1), 101-120.

the need to better coordinate investment across the engineering biology landscape and technology readiness levels. Furthermore, it highlights the importance of translational manufacturing research, which has traditionally been funded by EPSRC. UKRI budget allocations show that although EPSRC funding has been slowly increasing, its proportion of the total budget has been losing weight since 2021/2022 (data only available until 2024/2025)[4] as opposed to increases in more applied industry funding. We argue that the full benefits of engineering biology will not be reaped without first dedicating the appropriate support for manufacturing/scale-up research of biological solutions. We would note though that innovation is also needed for testing, scale up, and commercialisation of health engineering biology applications.

a. Take the EPSRC Future Targeted of Healthcare Manufacturing (FTHM) Hub, which is an example of the success of UKRI funding. The FTHM Hub includes research on the manufacture of promising cancer therapies ranging from Chimeric antigen receptor T-cell (CAR-T) therapies through to targeted drug therapies such as antibody-drug conjugates and cancer vaccines. It has provided a unique opportunity for the UK to take on a world-leading position for manufacture in the targeted healthcare sector, which is one of the key applications of engineering biology. The production of these therapies is highly complex, which means that current supply chain models can only handle a limited number of patients at the time. Failing to allocate enough investment to support more sustainable and cost-effective manufacturing of advanced techniques as well as associated supply chains, means that these will never be affordable enough to treat more than a few hundred patients a year. In addition, time and cost of travel to specialised centres can pose an economic burden to patients and carers and reduce access to treatment.

How should engineering biology be regulated?

2- As identified by Sir Patrick Vallance's Review of Pro-innovation Regulation of Technologies, there is a range of potential technological solutions in engineering biology that can solve the most pressing issues faced by society. However, some of these solutions and associated security measures do not currently align within existing regulatory limits – such as with the crossover of engineering biology and Artificial Intelligence (AI.)

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[3] https://www.gov.uk/government/publications/advice-on-engineering-biology/letter-to-the-prime-minister-on-engineering-biology-html

[4] https://www.ukri.org/wp-content/uploads/2022/06/UKRI-241023-BudgetAllocationExplainer2022To2025.pdf

An example of this is how DNA sequences can be obtained. Currently, it is possible to easily obtain DNA sequences from gene synthesis providers that encode for single proteins, such as toxins. Individually this may not be seen as unusual, but such genes can be combined with others in ways that generate potentially harmful functions. Furthermore, generative AI approaches could be used to create completely new functional sequences (de-novo) with potentially harmful effects, and yet with no obvious similarity to known harmful sequences. Some security measures to prevent these risks, like sequence screening for viral or pathogenic elements are already done by major providers such as GenScript[5], but they are dependent on prior biological knowledge. There is a need to develop more sophisticated algorithms to detect generative-AI sequences and their potential function, and then identify risk levels either in isolation or in combination with other functions. This can then be implemented at the point of ordering the DNA from gene synthesis companies, analogous to restricting the ordering of chemicals with potential uses in synthesis of harmful molecules. DNA orders should be accompanied by a simple to complete risk assessment validated by the registered/authorized manufacturing institution. Ultimately, the sequence and the context of usage must be screened and logged by gene synthesis providers. Some security measures such as licences to conduct de-novo protein design or licences for the relevant tools may be too limiting to innovation. Recently launched Regulatory Science and Innovation Networks may offer an opportunity to tackle these issues as well as alignment with regulatory frameworks for medicines (see recent MHRA regulatory reform[6]), the Responsible Research Innovation (RRI) framework, and GM risk assessments expected in academic institutions and industry. It is reassuring that the government has identified screening of synthetic DNA as a responsible innovation policy priority for 2024[7], but the potential to ignore the frameworks above and intend harm by creating new constructs, in the UK or anywhere else in the world, cannot be underestimated.

What are the possible barriers and limitations to good and effective use of engineering biology?

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[5] "Strengthening Security for Gene Synthesis: Recommendations for Governance", Amanda Kobokovich, Rachel West, Michael Montague, Tom Inglesby, and Gigi Kwik Gronvall; *Health Security* 2019 17:6, 419-429 (https://doi.org/10.1089/hs.2019.011)

[6] https://www.gov.uk/government/publications/implementation-of-the-future-regulation-of-medical-devices/implementation-of-the-future-regulations

[7] https://www.gov.uk/government/consultations/ai-regulation-a-pro-innovation-approach-policy-proposals/outcome/a-pro-innovation-approach-to-ai-regulation-government-response#executive-summary

Principle barriers and limitations include (i) Skills (ii) Feedstock and Data (iii) Public Opinion.

3- **(i) Skills**: According to the recent "Cell and Gene Therapy UK Skills Demand" Report the forecasted number of skilled workers in 2028 in bioprocessing roles (including manufacturing, supply chain and logistics, process development and total quality) will increase 54% to what was verified in 2023[8]. This report was based on a survey which included 90% of the industry's biomanufacturing capacity and has surfaced that there is a high level of concern to meet demands in manufacturing positions. It is important to indicate that this is only a subset of engineering biology applications in healthcare, without considering all other applications in sustainability, cellular agriculture or other areas. There are many essential skills required for engineering biology which include scale-up, process monitoring and control, process optimisation, data mining, mathematical modelling of biological systems, programming and process analytical technologies, to name a few. Current figures released on the number of PhD research graduates which embody some of these skills (process and chemical engineers, as well as production and manufacturing engineers) were only 250 in 2021/2022[9]. The recent announcement of two new Centre for Doctoral students focussed on engineering biology research is welcome, but it means that there should be no more than 150 graduates expected over the next four years. Although, there may be other way to progress into engineering biology roles such as upskilling from other positions, there does not seem to be a clear strategy on the National Vision for Engineering Biology on how demands in the sector will be met to harness the potential of engineering biology.

4- **(ii) Feedstock**: The UK needs to make sure that there is a constant supply and adequate amount of sustainable biomass feedstocks that can be used to manufacture bioproducts via engineering biology approaches. Larger companies such as Croda, Cellucomp and Fiberight are extracting fractions from various feedstocks (such as sugar beet pulp, paper waste, second generation lignocellulosic feedstocks etc) and subsequently converting these fractions into valuable biochemicals and materials with in-house technologies on a larger scale. More research is required to understand the potential of alternative domestic feedstocks for uses in engineering biology, and ensure their constant supply as feedstock production and yields may vary seasonally. Furthermore, understanding the regional landscape production of 'native' feedstocks will also ensure a constant supply and meet the demand for a UK bioeconomy. Feedstock production

[8] https://cgt.ams3.cdn.digitaloceanspaces.com/CGT-Catapult-Skills-Demand-Report-2023.pdf
[9] https://www.hesa.ac.uk/data-and-analysis/students/table-54

yield data, particularly for promising and emerging feedstocks such as seaweeds, are either difficult to obtain or are simply not presently available due to non-existent large-scale aquaculture facilities in the sector. With Government backing and financial investments to support an upscale of the aquaculture industry, production yield records can begin for the different commercial species of seaweeds that can be cultivated across the UK for applications in Engineering Biology. Additionally, technologies that have already been developed for feedstocks in current use across the UK may not be compatible with 'new' feedstocks, such as seaweeds, and their scale up potential needs to be better understood.

(iii) Public Opinion: As a naturally occurring resource around the UK coastline, seaweeds continue to gain recognition both nationally and internationally, as one of the most sustainable and energy efficient feedstocks for use within a circular bioeconomy. Seaweeds are known to contain a wealth of valuable compounds locked up within their structures, for applications in pharmaceuticals, nutraceuticals, food and cosmetics, or conversion into biofuels, yet to achieve these at scale requires large seaweed farms which will have a direct impact on coastal communities. The acceptance of the public is essential to deliver the full benefits of engineering technology solutions and the use of marine biomass as a feedstock illustrates this well: Biome Algae – a marine company, which specializes in farming and processing of local seaweed – decided to withdraw license applications to set up a seaweed farm at Gerrans Bay, due to local campaigning that argued against it due to impacts on local fisherman's livelihood and disturbing/affecting the natural landscape[10] .There is therefore a need to promote technology and encourage outreach activities to help gain public input towards responsible development and obtain a social licence from affected communities. To meaningfully engage, public and stakeholder engagement activities should consult on and unpack the impact of seaweed farms not just on marine biomass production, but on the affected community as whole, such as the impact on the economy and tourism.

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[10] https://www.falmouthpacket.co.uk/news/24032249.large-seaweed-farm-gerrans-bay-cornwall-withdrawn/