# Written evidence from Dr Stefanie Frank (UCL), Rita Morais (UCL), Dr Brenda Parker (UCL), Anca Tacu (UCL), Professor Brendan Wren (LSHTM) (ENB0029)

This submission has been prepared by Anca Tacu, Policy Adviser at the UCL Policy Impact Unit on behalf of Vax-Hub Sustainable and Vax-Hub Global. The response to this call for evidence on engineering biology aims to share a unique perspective which comes from bringing together research expertise in vaccine design and manufacturing technologies, and bio-integrated design as an interdisciplinary vehicle for incorporating sustainability principles and practices into vaccine manufacturing and facility design.

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## 2. What are the key applications for engineering biology?

In the context of vaccine development and manufacturing, engineering biology and genetic engineering offer new strategies for immunogen design and can contribute to the rise of next-generation vaccine platform technologies. New vaccine platform technologies have the potential to trigger stronger immune responses and enable the targeting of new pathogens, for a faster, more adaptable and efficient response to emerging diseases and improved preparedness for future outbreaks.

Engineering biology also enables the creation of innovative biomaterials customized for specific properties such as enhanced strength, biocompatibility, or degradability. This paves the way for sustainable alternatives to conventional materials and a circular bioeconomy through industrial symbiosis. The integration of biochemical engineering with molecular techniques creates the potential for scale-up, in order to generate meaningful quantities to address applications within the built environment or bio-based consumer products where volume is important. In future, we may wish to draw upon biohybrid, or animate materials which are responsive and adaptive to bespoke environmental challenges. These can be deployed in diverse fields, from architecture and industrial design to medicine [1].

## 3. How can Government policy support the development of engineering biology?

Although the Government has committed to spend £2 billion over the next years on engineering biology, not enough detail has been provided within the "National Vision for Engineering Biology" on how and for what initiatives this funding will be allocated.

The UK is a global leader in research and innovation, but challenges remain in terms of translating the scientific discoveries in a way in which these can be scaled up for manufacturing [2]. In relation to vaccine development, the gap between the initial discovery stages and manufacturing at scale is still significant. In order to bridge this gap, dedicated funding and establishing teams of experts who focus on the scaling up of lab discoveries are required.

Scaling up is particularly challenging for bio-integrated design for applications that rely on an environmental context as there are inherent limitations to lab-based research which cannot recreate the variability of outdoor conditions. For instance, the creation of engineered living materials would require a testing condition that enables interaction with humans, the microbiome and the surrounding ecology.

There is a need for investing in facilities where people can learn, test ideas and train on how to use equipment. Human capital is just as important as or even more important than assets as people working on applications of engineering biology need the confidence to develop and test new ideas. Lessons can be learned from the Bio Base Europe Plant, which is an independent facility with state-of the art equipment operating from lab level to a multi-ton scale and which focuses on process development, scale-up and custom manufacturing of biobased products and processes.

UK Biofoundries such as the London Biofoundry are well-equipped and important to support start-up companies. However, part of the expertise required is to understand that, when working with vaccines or other engineering biology applications, having the right equipment for scaling up is not sufficient. It is essential to understand the bio-physical interactions of the different components and how the material behaves when scaled up from millilitres to thousands of litres.

Working in engineering biology requires a particular set of skills and interdisciplinary expertise, including in integrated design where upstream, downstream or discovery work are not treated separately but in a joined-up manner which considers holistically the different parts of the manufacturing process. Specifically, more support is required for training and engagement with

those who work in molecular biology to increase awareness about scaling up processes for manufacturing. Not considering costs and feasibility of scaling up at the early discovery stages is not an effective approach as the whole process may end up having to be redesigned when moved to manufacturing. There is a need to consider 'design for manufacture' - for example choosing the cell line and expression system that is compatible with scale-up.

Long-term sustained funding for the development of multiple vaccine platform technologies, which can be quickly moved into large-scale manufacturing in the case of a disease outbreak, is very important to ensure resilience and increased ability to respond to future threats. Research undertaken within both Vax-Hub Global and Vax-Hub Sustainable focuses on multiple vaccine technology platforms which can be used to improve existing vaccines and produce new vaccines. This is important in terms of building capabilities to respond to future disease outbreaks and pandemics, particularly in LMICs. Focusing on a single platform technology (e.g. mRNA) risks limiting the ability to respond to pathogens that require a different type of vaccine platform, for example glycoconjugate vaccines against most bacteria pathogens. This will become increasingly important with increasing antibacterial resistance and as climate change continues to increase the prevalence of vector-borne disease (e.g. malaria, dengue) [4].

## 5. What are the risks posed to society by engineering biology?

Biosafety should be a key consideration for all engineering biology applications. Although engineering biology has the potential to address many of our current societal challenges, the ability to manufacture at scale brings risks through potential contamination of water or food crops for example. Various biocontainment strategies have been developed but they have certain issues that need to be addressed. Characterisation of the effectiveness of biocontainment and application to large scale manufacturing is still lacking [5]. When biocontainment systems are used in large scale production, the metabolic burden on the host cells must be considered and the associated costs that come with defined media and addition of certain nutrients. Vaccine development and engineering different vaccine platform technologies may have dual-use potential through informing or enabling pathogen engineering, which may increase the risk of deliberate, anthropogenic biological events [6]. International agreements on biosafety are particularly important in the current geopolitical climate.

## 6. How should engineering biology be regulated?

The benefits of Biological Engineering outweigh theoretical consequences of newly engineered microbial cells that may have advanced practical benefits for

therapeutics, diagnostics and vaccines. Current regulation including Genetic Manipulation Advisory Groups regulated through HSE would seem sufficient.

Vaccine regulation is well-established and conservative as safety is paramount. Given the rapid advancement of new vaccine technologies (e.g. future increased use of combination vaccines, new ways of vaccine delivery), more flexibility on the part of vaccine regulators is likely to be required in order to support innovation in this space.

In terms of new biomaterials, these are very difficult to compare adequately to conventional materials in terms of their performance as they often perform more than one function. This has significant regulatory implications as it is challenging to prove the same level of performance and to decide which regulatory pathway to follow. This contributes to high barriers to bringing new materials to market, alongside the risk-averse culture in industry. When it comes to adopting more sustainable types of plastic, similar barriers exist due to the costs attached to adopting new types of plastic and the time required to obtain the regulatory approval. Regulators should adopt a more flexible and agile approach when considering how to support new more sustainable materials. One solution could be adopting a fast-track approval process for innovative, low-risk biological and sustainability-enabling solutions; this could lower the time to market for new products while still adhering to high standards of consumer and of consumer and environmental safety [3].

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

Engineering biology, as opposed to other branches of engineering, presents the issue of outputs which don't behave in a predictable manner. Particularly when considering molecules, it is challenging to predict how they will behave in a manufacturing environment. Adopting a 'design for manufacture' approach, which is more commonly used in construction, could be part of the solution.

As engineering biology has been advancing and the number of vaccine candidates has increased, one of the bottlenecks is in relation to the animal models required to test the immunogenicity, feasibility and efficacy of vaccines. Although some cell-based models exist, they cannot replace animal models in understanding the complexity of the immune response.

In terms of bio-synthesised materials (e.g. biomaterials grown from a particular type of bacteria or algae), one of the main challenges is being able to test and evaluate how the materials behave in the real world. There is a need for multiple disciplines to work together on understanding how different organisms

used for biomaterials interact with humans and other animals in real world scenarios.

Another significant limitation may be poor communication with the press and public trust in applications of engineering biology. Public perceptions of engineering biology influence public uptake of products and applications. The public are more distrustful of terms and processes that they perceive to be artificial or unnatural [7]. Whether it is new vaccines or new materials, having the public's trust is very important if these are to be adopted on a large scale. Consequently, efforts will have to be directed towards increasing public literacy in engineering biology so people can feel empowered to make informed decisions.

The current tools to evaluate the sustainability of engineering biology applications have limitations; it is challenging to measure the environmental footprint of vaccine ingredients and bioprocessing more broadly. The inherent complexity of calculating the environmental impacts of biological raw materials (e.g. glucose as a carbon source) are dependent on the origin and method of agriculture. We also lack the ability to adequately compare systems that have different outputs – for instance multi-functional materials or vaccines can have significant behavioural or social impacts that are hard to embody by merely comparing manufacturing methods. It is important to increase environmental literacy and have more refined tools for measurement; for example, one of the research areas Vax-Hub Sustainable will be exploring is how to enable more precise life cycle inventories reflective of the actual materials used in bioprocesses.

Price gaps between a bio solution and less sustainable alternatives pose a significant barrier to the development and commercialization of innovative solutions [3]. This is particularly notable because the environmental benefits of more sustainable solutions (e.g. increased biodiversity, CO2 capture, and bioremediation properties) are not fully accounted for economically. Additionally, less-developed bio solutions may face higher expenses compared to alternatives due to their limited scalability, thus missing out on the potential economies of scale. This can limit the adoption of innovative solutions in the market. Active government support using levers such as tax incentives and subsidies, which take into account environmental benefits and avoided emissions, is required to support the uptake of new innovative low-carbon bio-based solutions and to create a more level playing field with products that already exist on the market [3].

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