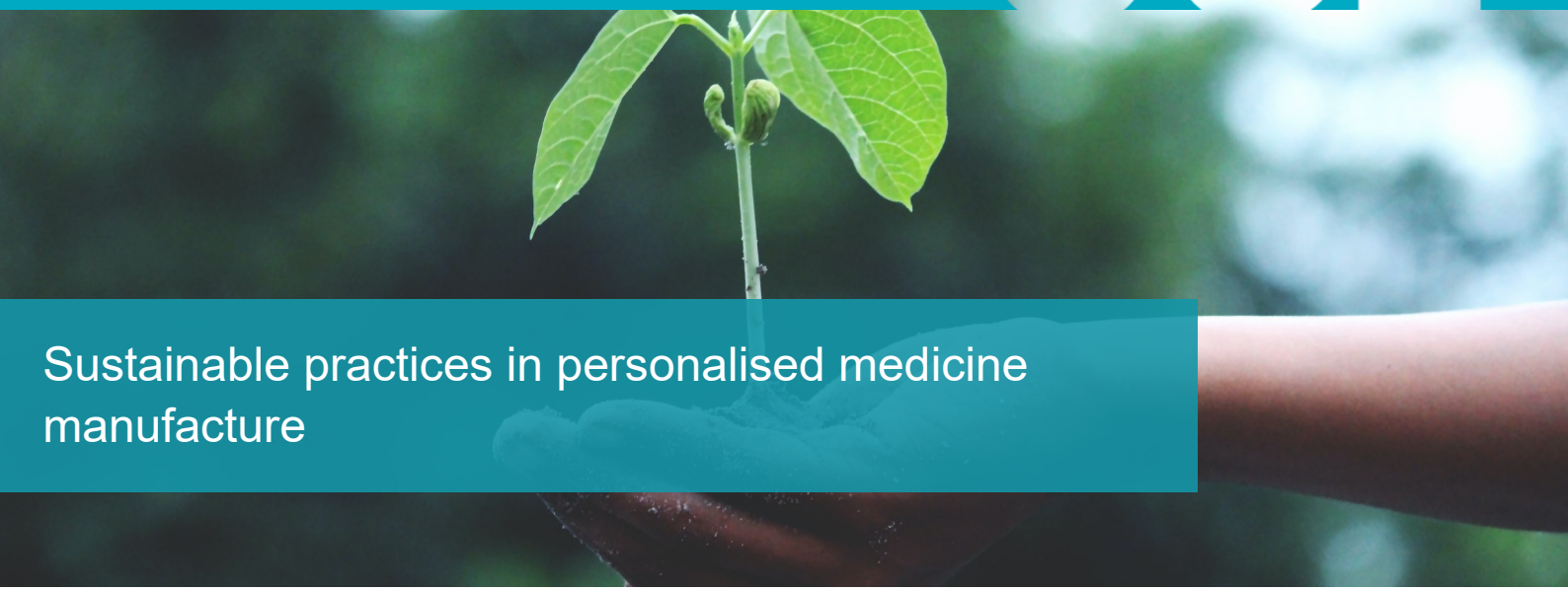


Sustainable practices in personalised medicine manufacture

On 01 July 2022, the Future Targeted Healthcare Manufacturing Hub (the 'Hub') held an online sandpit workshop to outline the current and future priorities in sustainable practices for manufacturing personalised medicines, and how the Hub should integrate and advance these in the next phase of their research. The workshop brought together the Hub team with a range of national and international stakeholders involved in personalised medicine development, manufacturing, delivery, and policy.

Context

Whilst new and innovative personalised medicines (namely, cell and gene therapies and stratified proteins) are improving the lives and health outcomes of millions of people around the world including those with previously unmet needs, these gains could be quickly offset by the greatest threat to global public health: our changing climate. According to the Intergovernmental Panel on Climate Change (IPCC) if emissions continue unabated, by 2050 we can expect to see approximately 250,000 additional deaths per year from malnutrition, malaria, diarrhoea and heat stress. To avert these catastrophic health impacts, we must limit the global temperature rise temperature rise to 1.5°C.[1] Although some further increases to global temperatures are guaranteed from historic greenhouse gas emissions, it is still possible to avoid the worst impacts on human health and the environment. If we are able to reduce and mitigate greenhouse gas emissions to close to zero by 2050, we will be able to prevent the worst scenarios of catastrophic climate change.

To reach ambitions for a 'net zero' future, urgent action is needed from every sector, including the pharmaceutical industry. Although healthcare is often overlooked, activities from the UK's healthcare system currently contribute around 5% of the UK's carbon emissions, with medicines and chemicals responsible for a fifth of this.[2] The global pharmaceutical industry is not only a significant contributor to climate change, but it is also more polluting than the global automotive production sector.[3] Fortunately, extensive work is already underway to understand and mitigate the pharmaceutical sector's impact on the environment, and within that, there are significant opportunities for biopharmaceutical and

Key points

1. **Carbon emissions**: addressing carbon emissions for PMs are likely to have the greatest impact on sustainability targets. Little is known about scope 3 (supply chain) emissions for a PM so mapping these would be valuable.
2. **Circular economy:** single-use plastics have increased in prevalence and very little is reused or recycled, due to sterilisation needs. Working with other sectors to recycle these plastics would be very valuable.
3. **Waste:** reducing waste through process intensification will lead to more sustainable manufacturing. A mapping exercise of the different process steps and how these can be intensified would be of value.
4. **Biodiversity:** work is needed to understand the impacts of manufacturing personalised medicines on biodiversity as little is currently known about this.

The Future Targeted Healthcare Manufacturing Hub

The current "one-size-fits-all" approach to drug development is being challenged by the growing ability to create stratified and personalised biological medicines for groups of patients and even individuals. Many of the approaches in this new class of medicines use advances in gene editing technology and have the potential to cure, and not just treat, patients.

The Hub is addressing manufacturing, business and regulatory challenges to ensure that new targeted biological medicines can be developed quickly and manufactured cost-effectively.

"We have seen how important it is to have established and leading bioscience capability in the UK to meet the challenge of the now. The FTHM Hub has the skills in multiple disciplines, the bio-processing insights and is developing the technologies and training the people to help meet these future challenges".

- Dr Mark Carver, Chair, Hub User Steering Committee

personalised medicines to lead the way in sustainability. This is due to in large part to the novelty of the products, potential to adopt innovative manufacturing methods and the capabilities to manufacture small amounts of product, close to the patient thereby potentially reducing emissions associated with the supply chain.

The workshop

The aim of this workshop was to obtain a clear understanding of the current and future environmental sustainability challenges in personalised biological medicine (cell and gene therapies and stratified proteins) manufacturing and understand which of these should be prioritised in the Hub's next programme of research once the current Hub draws to a close at the end of 2023. For this workshop, the following environmental sustainability categories were considered, in line with those used by the Engineering and Physical Sciences Research Council's (EPSRC) first sustainable manufacturing Hubs funding call.[4] These were:

- reducing carbon emissions
- resource efficiency and circular economy
- waste or pollution elimination
- protecting and enhancing the natural environment and biodiversity

To prepare participants for the ensuing discussions, presentations were provided by:

- The Hub's co-directors, Suzy Farid and Paul Dalby, who informed participants of the Hub's achievements to date, and some initial ideas on research grand challenges for the next Hub;
- Karen Wilkinson (the Knowledge Transfer Network, KTN) and Steve Hoare (the Association of the British Pharmaceutical Industry (ABPI) who spoke about work ongoing in the Medicines Manufacturing Innovation Partnership (MMIP) to understand the sustainability needs of the sector and projects developed to meet these;
- Peter Morgan (NHS England), who provided an overview of the NHS Delivering a 'Net Zero' National Health Service strategy to become net zero by 2040 for the emissions the NHS controls directly, and net zero by 2045 for the emissions the NHS has the ability to influence;
- David Sexton (Cell and Gene Therapy Catapult, CGTC) who shared insights from the work ongoing in the Catapult to enhance their environmental sustainability; and
- Jason Snape (AstraZeneca) who shared highlights from the organsation's Ambition Zero Carbon' strategy to eliminate emissions by 2025 and be carbon negative across the entire value chain by 2030.

This report summarises the discussions around the four environmental challenges, where there are gaps in evidence, and the types of research activity it would be helpful for the Hub to carry out to help fill these in a future research programme.

Carbon emissions for personalised medicines manufacture

Participants shared that relative to other types of medicinal products and biological therapies (e.g. monoclonal antibodies) relatively little is known about the carbon emissions associated with manufacturing personalised medicines. Further work was required to understand emissions associated with different processes and inputs for personalised medicines. However, there were some areas highlighted that may account for a large proportion of emissions including the prevalence of single-use components in manufacturing, and the heating, ventilation, and air conditioning (HVAC) of facilities in which these products are made. Participants shared that work to understand more about the

following areas would be helpful:

- Impact of different types of product: Understanding more about the relative emissions from manufacturing processes to produce types of product (e.g. mRNA, proteins, cell therapies etc.) would be helpful. This would not only inform process design choices made by manufacturers but could assist with reporting for procurement purposes, e.g. the NHS Net Zero strategy has set out a requirement for suppliers to publish a carbon reduction plan for their UK Scope 1 and 2 emissions by 2024. In this respect, the Hub could lead on life cycle assessments (LCA) for a range of different product types, mapping out the various processes used to make them, which could help inform process design choices made by manufacturers. Collaboration with others including the Cell and Gene Therapy Catapult on specific case studies, e.g. CAR T-cell therapies, would be informative and would minimise duplication of effort.
- Supply chain (scope 3) emissions: These are particularly challenging to map due to the need to gather data from a range of suppliers which may have been calculated using different methodologies. Obtaining carbon footprint reports from suppliers and working with them to harmonise metrics would be incredibly useful.
- Applying LCA approaches to understand the impacts of not only the manufacturing of personalised medicines, but also their relative impact on activities as part of new modes of healthcare provision (e.g. will patients have to travel further to specialist hospitals, and accounting for time under surveillance in hospital beds after patients have received certain therapies, for example CAR T-cell therapies).

Resource efficiency and the circular economy for personalised medicines manufacture

Participants shared that the current manufacturing processes used to produce personalised biological medicines have extremely low process efficiencies and so gains here could have considerable impacts on the overall environmental sustainability of these products. Additionally, the industry had tended toward single-use plastics in recent years, with very little of these reused or recycled, largely due to sterilisation requirements. Participants shared that work to understand more about the following areas would be helpful:

- A better understanding of the quantity and composition of the waste generated from manufacturing different products is needed. The Hub could develop digital models and tools, coupling with LCA to assist decision-making.
- The volume of single-use plastics being used in the sector and possible routes for recycling or re-using the waste created. Since plastic waste for producing personalised medicines is similarly contaminated to hospital waste, it would be relevant to investigate its recycling in collaboration with/informed by partners operating in the NHS. Work may be required with policymakers to encourage and incentivise recyclers to process the waste.
- Water recycling would be of interest, particularly true in areas prone to drought. In this respect, the Hub could collaborate with membrane suppliers working on water recycling mechanisms, for example, Dupont, to apply these technologies to water waste from personalised medicines manufacture.

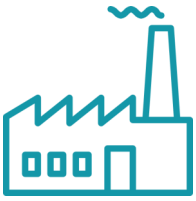
Waste or pollution elimination for personalised medicines manufacture

Participants noted the value of the Hub's focus on process optimisation and intensification and felt that this aspect of the Hub's research would be important to continue in the next phase to help manufacturers reduce the amount of waste produced through more efficient use of resources. The Hub could conduct a mapping exercise to determine which

Participant list by organisation

The workshop brought together 17 participants from the following organisations:

- The Association of the British Pharmaceutical Industry (ABPI)
- AstraZeneca
- Biopharm Services
- The Cell and Gene Therapy Catapult (CGTG)
- The Knowledge Transfer Network (KTN)
- The Engineering and Physical Sciences Research Council (observer)
- Innovate UK
- NHS England
- Sartorius
- Univercells
- University College London (UCL)



Scope 1 emissions
Direct emissions from owned or controlled sources

Scope 2 emissions
Indirect emissions from the generation of purchased energy consumed by the company

Scope 3 emissions
All other indirect emissions that occur in a company's value chain

manufacturing steps are most suitable for intensification and for continuous manufacturing. Additionally, participants felt the following areas could be explored:

- In addition to the volumes and types of waste produced for manufacturing different therapies, it would be useful to gain a better understanding of the costs of eliminating waste, which are not well known.
- It has been estimated £300 million of NHS prescribed medicines are wasted each year. It would be interesting to understand the volume of personalised medicines that are wasted since the least sustainable medicine is one that is never used. It would also be interesting to conduct studies to understand the impact of extending the expiry date on personalised and biological medicines, and also for the components used to manufacture them, and work to understand what the regulatory implications of this might be.
- A reduction in the amount of water wasted, either through intensification or recycling, would be impactful, especially in regions where water is scarce.

Protecting and enhancing the natural environment and biodiversity for personalised medicines manufacture

Participants agreed that this was the least explored area of the four environmental sustainability categories and so work to understand the impact on the natural environment of the full product lifecycle for personalised medicines using an LCA approach would be of value. Reducing the release of antibiotics, and nitrogen-, sulfur-, and phosphorus- containing compounds would be of particular importance to address due to their potential to impact biodiversity.

Conclusion and next steps

Significant work is already underway by many in the biopharmaceutical sector to address carbon emissions and reduce the impact on the environment from manufacturing medicines. In this respect, collaboration to understand and meet net-zero goals is vital to reduce the risk of duplication of effort and bring the sector towards net-zero operations more rapidly. Businesses are likely to have the most impact in reducing carbon emissions through better process and facility design and through reducing waste through process intensification and recycling. Using LCA approaches to understand the relevant impacts of manufacturing and healthcare provision for personalised medicines will be vital. The Hub will use the ideas generated in this workshop to inform the activities in their research proposal for the 'Hub 2', which will continue and build on activities from the first research cycle. This proposal is being developed in the Summer/Autumn 2022.

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Our research

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To find out more about the FTHMH, please visit: www.ucl.ac.uk/biochemeng/hub

Contributors

Suzy Farid (s.farid@ucl.ac.uk), Professor of Bioprocess Systems Engineering, UCL Biochemical Engineering; Paul Dalby (p.dalby@ucl.ac.uk), Professor of Biochemical Engineering and Biotechnology at UCL; Catarina Pereira Galo Neves, PhD candidate UCL Biochemical Engineering; Penny Carmichael (p.carmichael@ucl.ac.uk), Policy Engagement Specialist in the PIU.