Manufacturing Biological Medicines

January 2020

What is a biological medicine?

A biological medicine, or biopharmaceutical, is any medicinal product manufactured using a living organism.

Biological medicines are designed to interact with specific targets in a patient's body. This leads to a greater chance of the medicine having the desired effect against a disease and results in fewer side effects as compared to traditional pharmaceuticals.

Some biological medicines mimic proteins which are missing or faulty in the patient's body, for example insulin for the management of diabetes. Other biological medicines trigger an immune response in the patient's body, for example vaccines or immunotherapies for the treatment of cancer.

How are biological medicines made?

Unlike traditional pharmaceutical products that are made using chemical synthesis, biological medicines are made using biomanufacturing. In this process, the medicinal product is derived from, or manufactured by, living cells. Biological medicines are structurally much larger and more complex than traditional "small molecule" pharmaceuticals, meaning they are more challenging to manufacture and characterise.

How are biological medicines regulated?

Manufacture of biological medicines is rigorously controlled and highly regulated. Manufacturers must demonstrate that all aspects of the manufacturing process comply with safety and quality standards set out under Good Manufacturing Practice (GMP). In the UK, the Medicines Healthcare Regulatory Agency (MHRA) is responsible for enforcing GMP.

Before a biological medicine can be sold in the European Union, it must receive approval from the European Medicines Agency (EMA). Health organisations and sector industry associations have called for regulatory alignment with the EU post-Brexit to reduce potential trade hurdles and ensure UK patients can continue to access safe and effective medicines.[2]

Biological medicines in numbers

$275bn

global total annual revenue of the biopharmaceutical sector in 2018[1]

12%

average annual growth of the global biopharmaceutical sector[1]

40%

percentage of drugs in development which are biopharmaceuticals[6]

316

number of individual biopharmaceutical products with current active licenses[6]

"Pharmaceuticals have a higher output than most other sectors of the economy. On indexed output per hour, pharmaceuticals exceed the output of other major sectors such as communications, computing, electrical and optical, transport, manufacturing, professional services, and financial services"

Life Sciences Industrial Strategy, 2017[9]

"The Government has an opportunity right now to get ahead of international competition. It can, and must, take bold steps to secure the future growth and expansion of the life sciences sector. This is even more vital as the UK prepares for life outside the European Union"

House of Lords Science and Technology Committee, 2018[11]

The UK pharmaceutical sector

The pharmaceutical sector is one of the UK's most productive industries.[3] In 2018, the UK pharmaceutical sector (including small molecules) generated a turnover of £50bn and employed 121,000 people.[4] Biological medicines represent an increasingly large proportion of goods produced by the pharma sector and already comprise eight out of the top ten selling medicines by revenue.[5] In 2018 40% of pharmaceuticals in clinical development globally were biological medicines,[6] and by 2024 it is projected that total sales of biological medicines will equal those of conventional small molecule pharmaceuticals.[7]

The UK leads the EU in terms of the number of companies developing biological medicines,[8] and has the strongest product pipeline in the EU in terms of the number of products in development. Compared to the US, life sciences discovery R&D in the UK is funded at approximately half the value per capita[9], but research productivity (in terms of public spend per weighted publication) is twice as great as that in the US. Overall the UK has the highest gross value added per public spend globally.[8]

The skills challenge

A highly skilled workforce is essential to develop, manufacture and deliver innovative biological medicines at scale and to meet the growing demand for biomanufacturing. The UK's world-leading universities are vital in delivering the necessary pipeline of skilled workers through university-based training and research.

UCL is a world leader in biotechnology research in the field of engineering, ranking second in the UK and fourteenth globally.[10] Its Department for Biochemical Engineering is home to the Advanced Centre for Biochemical Engineering (ACBE), the largest academic centre for biomanufacturing research in the UK. The ACBE's reputation for excellence is in developing the understanding to convert novel biological discoveries into commercial products safely, sustainably and cost-effectively.

UCL biomanufacturing research

In addition to the ACBE, UCL's Department of Biochemical Engineering hosts two EPSRC-funded 'Future Manufacturing Research Hubs'; part of a strategic Government investment to ensure UK manufacturing industries are ready to respond to new and emerging opportunities. The Hubs are called the Future Targeted Healthcare Manufacturing Hub (FTHM Hub) and the Future Vaccine Manufacturing Research Hub (Vax Hub). The two Hubs are addressing challenges relating to the biomanufacture of personalised medicines and vaccines.

UCL researchers in the Advanced Centre for Biochemical Engineering

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 exciting new class of medicines take advantage of advances in gene editing technology and have the potential to cure, and not just treat, patients.

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

- "Just-in-time" manufacture of biological medicines to deliver personalised treatments to patients;
- Formulation strategies for stable combination protein therapeutics to target the underlying cause of disease in each patient;
- Reimbursement strategies for personalised medicines to ensure long-term economic feasibility;
- Development of advanced software tools to enable manufacturers improve decision-making; and
- Regulatory pathways for targeted biological medicines are being assessed along with their impact on manufacturing strategies.

With over 40 partnering organisations spanning academia, industry and policy-making, the Hub has enormous convening power which it is using to drive forward the agenda for research and innovation in targeted biological medicines. Current FTHM Hub projects include:

- Development of new manufacturing platforms for personalised cancer treatments;
- Analysis of the regulatory pathways for cell and gene therapies considering factors such as marketing application review times and post-marketing requirements;
- Analysis of the National Institute for Health and Care Excellence (NICE) approach to appraising CAR T-cell therapies, including long-term feasibility;
- Supply chain analysis of centralised versus bedside manufacture of personalised therapies; and
- Economic analysis to investigate the consequences of switching to scalable processes for viral vectors. This work is in collaboration with the BioIndustry Association Manufacturing Advisory Committee and fed into an MMIP business case on "A UK Strategy for the Manufacture of GMP Viral Vectors".

"The Hub will work to help the sector bridge the gap from academia to industry and drive forward with bioprocessing technologies and get them into industrial applications."

- Dr Oliver Hardick, CEO and Founder, Puridify Ltd

Professor Nigel Titchener-Hooker
Hub Director, UCL

Professor Suzy Farid
Hub Co-Director, UCL

Professor Paul Dalby
Hub Co-Director, UCL

For more information visit:

https://www.ucl.ac.uk/biochemical-engineering/research/research-and-training-centres/future-targeted-healthcare-manufacturing-hub

UKRI Engineering and Physical Sciences Research Council

Professor Martina Micheletti
Hub Co-Director, UCL

Professor Sarah Gilbert
Hub Co-Director, University of Oxford

The Future Vaccine Manufacturing Research Hub

The Vax Hub is funded by the Department of Health and Social Care's UK Vaccine Network which makes targeted investments in vaccines for infectious diseases that have the potential to cause an epidemic.

The Vax Hub is designed to bring together academics, manufacturers and policy makers to consider and devise novel ways to develop new vaccines for pandemic diseases in low and middle-income countries (LMICs).

Since many vaccine manufacturing processes are designed for developed, high income markets, they are ill-suited or too costly for use in LMICs. As such, the Vax Hub is working directly with LMIC manufacturers to develop processes that improve the local response to serious diseases before they become global emergencies. Vax Hub is addressing the following vaccine manufacturing challenges:

- Accelerating the time to market for vaccines;
- Guaranteeing the supply and improving the shelf-life of vaccines;
- Reducing risk of failure when different vaccine types are transferred from research labs to clinical development, and when scaling up manufacture;
- Mitigating cost as much as possible – which is essential for LMICs; and
- Providing better protection from pandemic threats through development of rapid response "make it when needed" vaccine manufacturing solutions.

The impact of this Hub will be felt internationally and the outputs of the Vax Hub reach the most vulnerable populations in LMICs, especially children. Current Vax Hub projects include:

- Development of a single dose rabies vaccine;
- Pioneering new thermostabilisation technologies to avoid the need for cold-storage;
- Development of an effective malaria vaccine, work being undertaken in collaboration with the Serum Institute of India; and
- Development of a low cost Dengue Fever vaccine, work being undertaken in collaboration with PT Biofarma Indonesia.

"We are very excited to be a translational spoke within the Vaccine Manufacturing Hub and to collaborate with the team on developing new technologies to improve the expression of our Dengue vaccine, shorten development times and benefit from economic models to achieve low costs."

- PT Biofarma Indonesia

For more information visit:

https://www.ucl.ac.uk/biochemical-engineering/research/research-and-training-centres/vax-hub

Engineering and Physical Sciences Research Council

UKaid from the British people

Department of Health & Social Care

References

1. Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, BioPlan Associates Inc., 2018.
2. Brexit – medicines, medical devices and substances of human origin, House of Commons Health and Social Care Committee, 2018.
3. Office for National Statistics, UK Productivity Introduction: April to June 2017, (October 2017), p4
4. Bioscience and health technology sector statistics 2018, Office for Life Sciences, 2019.
5. "Top 15 Best-Selling Drugs of 2018". GEN - Genetic Engineering and Biotechnology News
6. Walsh, G.; Biopharmaceutical benchmarks 2018; Nature Biotechnology; 2018; vol 36; pp 1136–1145.
7. EvaluatePharma World Preview 2019, Outlook to 2024
8. Site Selection for Life Sciences Companies in Europe 2018, KPMG, 2019.
9. UK Life sciences: industrial strategy, 2017
10. The Academic Ranking of World Universities (ARWU), Shanghai Ranking 2019.
11. Life Sciences Industrial Strategy: Who's driving the bus?, House of Lords Science and Technology Committee, 2018.