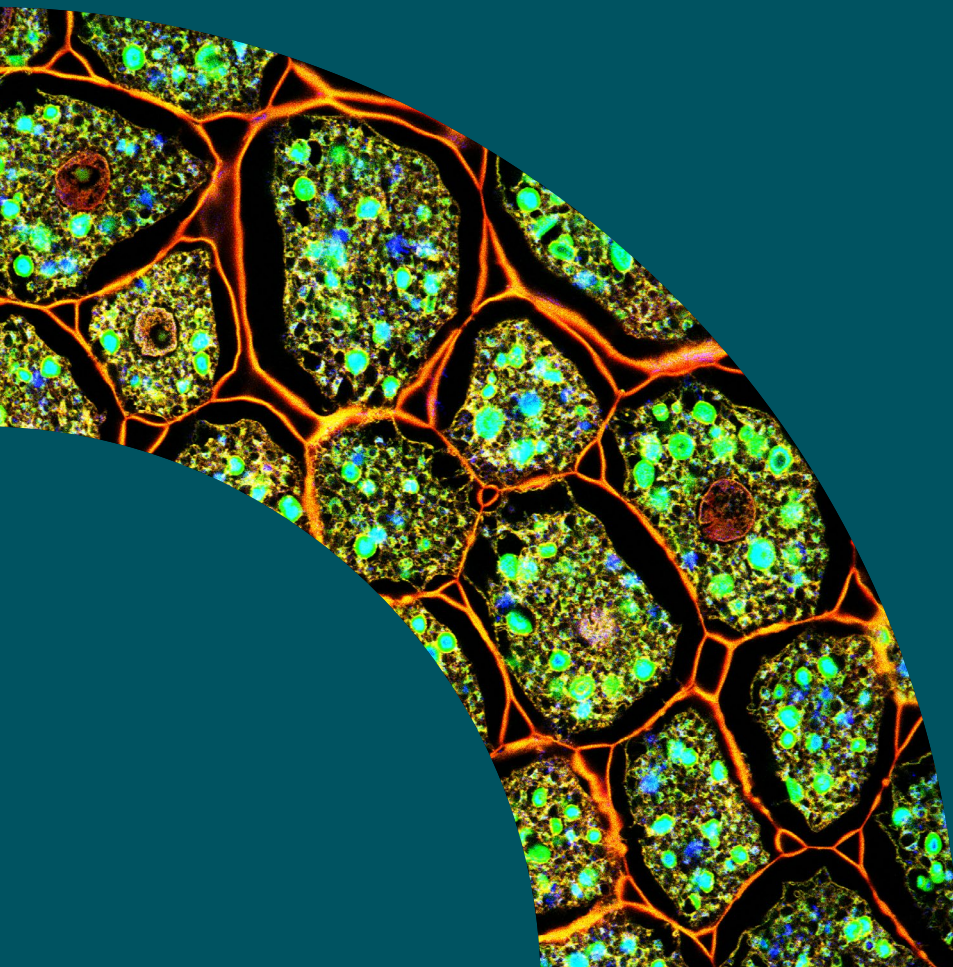


HEALTHCARE TRENDS

Introduction to the manufacturing of biologics



blue latitude^o
health

Introduction to the manufacturing of biologics

Ditte Funding, Blue Latitude Health

The last decade has seen the rapid growth of biologics in the pharmaceutical market, making them a key sector to watch in the coming years. Biopharma made up 22% of big pharma companies' sales in 2013, with this number being expected to rise to 32% of sales by 2023. With the growing popularity of these products, it's important to understand the opportunities and threats they present to pharma companies.

[Associate Consultant Ditte Funding](#) takes us through how biologics are made, what makes them unique, and what it all means for pharma companies.

What is a biologic?

Before looking at how to manufacture them, it's important to first understand what a biologic is. The definition of a biologic isn't always clear, and what's considered a biologic is constantly being updated and tweaked as new products are introduced to market. However, the broad definition of a biologic is they are created by either a microorganism or a mammalian cell, and are large, complex molecules; the majority of which are proteins or [polypeptides](#). [Examples of biologics](#) include blood or blood products, gene therapies, vaccines, and cell therapies.

There is a significant distinction that needs to be made between traditional small molecule pharmaceuticals (such as aspirin), and biopharmaceuticals. Biologics differ from small molecule drugs in their cost, production, administration, and clinical efficacy. Small molecule drugs are usually chemically synthesised, simple, and have a very well-defined structure. Whereas biologics, or large molecule drugs, are difficult to define and characterise.

“Biologics present great value as they are highly specific molecules that tend to target more difficult to treat populations; it seems that biologics may become a primary tool for targeting hitherto untreatable diseases.”

However, in order for biologics to be widely used treatments in the future, they must be manufactured at the right cost and the right scale.

Introduction to the manufacturing process: why is it unique and complex?

Biologics are much harder to manufacture than chemical drugs as they are extremely sensitive. Their [immunogenicity](#), adverse events, and efficacy can all be affected by even the slightest process change because a biologic is defined by its process. As such, the manufacturing process has to be carefully designed and closely monitored at every step in order to ensure correct product identity. [This makes it extremely expensive](#). For example, it [costs \\$200 – 500 million to build a large-scale biotech facility](#) versus \$30 – 100 million to build a small molecule facility.

To highlight the complexity of manufacturing even further, there are key metrics that the process must meet. Is the end purity high enough? If the

product is going into a human, it needs to be 99.9% pure at the end. Is the process robust? Meaning, do you get the same output when you run it the first time as the hundredth time? Is the process economically viable?

The process engineer designing the process will often have to design it very early in the development stages. They work under a tight time frame with a lot of uncertainty in order to get to market as soon as possible. Under these circumstances, the process often ends up being the first workable solution, rather than the perfect solution.

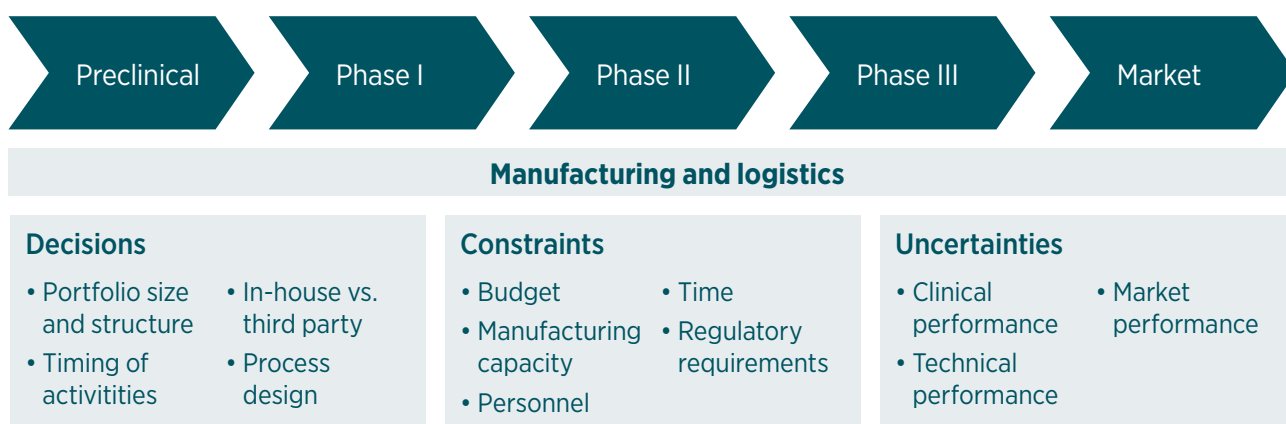
Once a process has been decided, it is extremely difficult and costly to change. This introduces yet another complexity unique to the manufacturing of biologics: it's extremely difficult to scale up or scale out. This means that it's challenging to change the volume of product produced once the process has been designed and the manufacturing plant built. This makes accurately predicting the market share early on incredibly important - it is expensive to have equipment sitting idle, but you also don't want to have a supply shortage.

The manufacturing of biologics is highly specific. It requires a lot of very skilled technicians defining process steps with very precise parameters and operating expensive equipment. However, the complexity of the process also gives pharma companies some security as it is extremely difficult for competitors to recreate the process and impossible for them to manufacture an identical biologic. [see page 4]

What does this mean for pharma companies?

The complexity of the manufacturing process has a significant impact on pharma companies developing biologics. With [biopharma growing at 8%](#) per year, double that of conventional pharma, it is now a significant area of growth for most pharma companies.

The manufacturing process affects our clients' competitive advantage, impacting the selling price, profit margin, and time to market. As illustrated in the diagram below, manufacturing influences the whole development process of a biologic from pre-clinical to market.



The impact on marketing and the BLH approach

BLH has worked on biologics across therapy areas. Our understanding of process engineers developing workable yet limited solutions has tailored our approach to biologics.

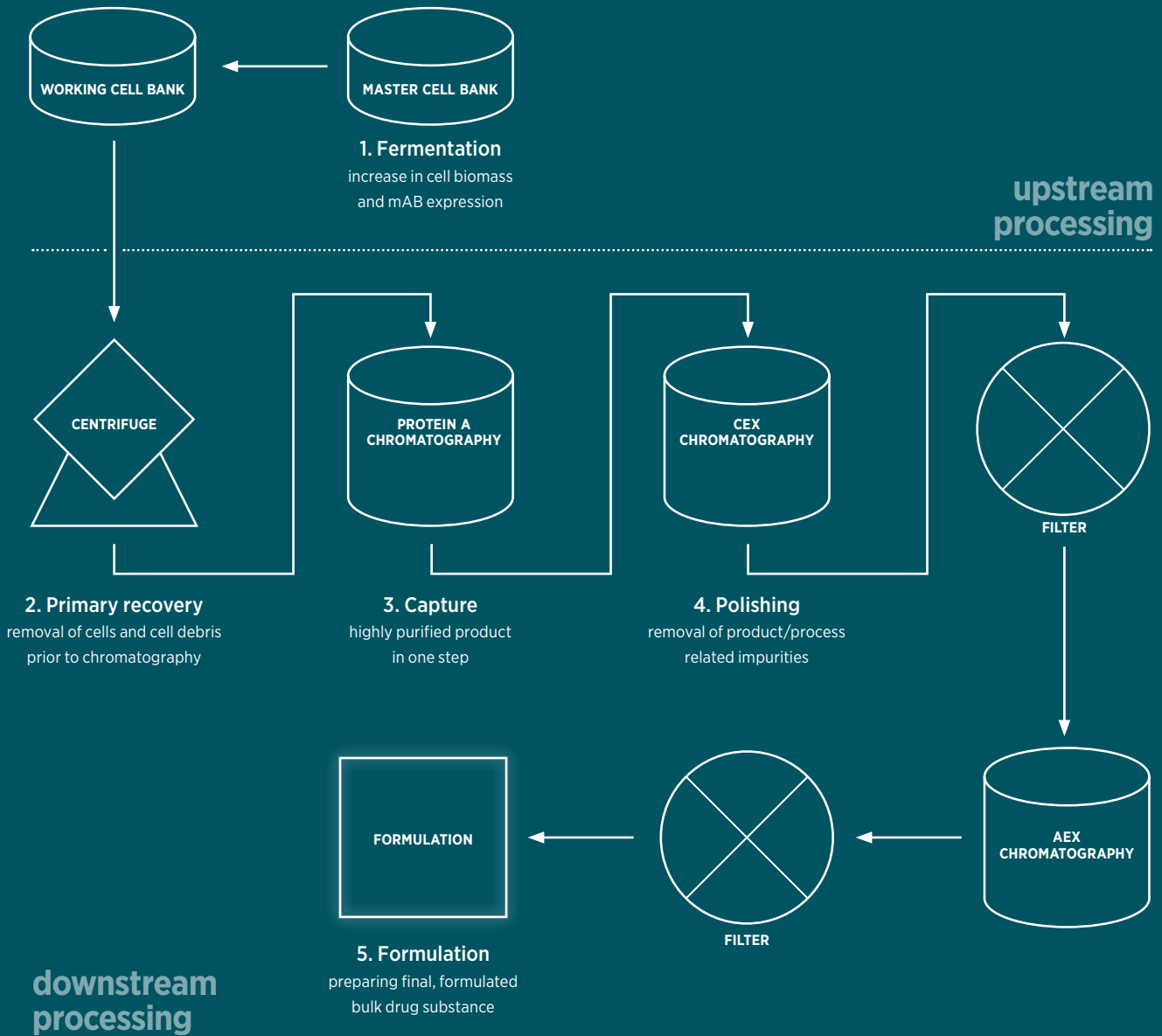
When working with a biologic, it's impossible to ignore the manufacturing process. It feeds into determining the [launch strategy](#), understanding the [competitive market](#), and the threats posed to [established products](#). An awareness of the strengths and weaknesses the process presents is essential when

determining the most successful marketing strategy.

The complexity of the manufacturing process is both one of the largest competitive advantages for our clients, as it is difficult for competitors to replicate a process, as well as one of the biggest challenges. Remembering to consider manufacturing when developing brand strategies for biologics ensures the creation of more robust and bespoke plans. For more on how we can help your brand tackle these challenges, get in touch with us at hello@bluelatitude.com. ■

Manufacturing of Biologics

An overview of a typical process



Key process impurities

- Host cell protein
- Aggregates
- DNA
- Cell Debris

Constant process considerations

- Flow rate
- pH
- Temperature
- Media
- Good manufacturing processes is a regulatory requirement
- Cleaning of the of equipment after each batch yield
- Purity - contaminants