Adapting to Supply Chain Issues Surrounding Antibody-based Therapy Production

The complexity and diversity of antibody-based therapies have been increasing with the growing understanding of the intricate mechanisms involved in immune responses, the discovery of novel therapy targets and the development of new technologies for antibody production. As a result, the biopharmaceutical industry has placed greater significance on advancements in manufacturing and collaborations within the supply chain. However, introducing new products or materials into a pre-existing process can be time-consuming and costly, as regulatory agencies must be notified and the entire manufacturing process reapproved.

Better access to innovative purification materials is crucial for delivering new antibody therapeutics to market, and the patients who need them. To overcome regulatory hurdles and adopt new materials into current processes with greater efficiency, the biopharmaceutical industry is exploring various strategies.

In this article, Aaron Moulin, Field Application Specialist at Purolite, discusses the need to establish robust supplier networks that will support streamlining biologics development and manufacturing processes. He also explores some of the emerging purification challenges associated with developing novel antibodies, emphasizing the importance of implementing a quality-by-design (QbD) approach when adopting new resin technologies.

Finding Support Within a Robust Supplier Partnership

The ongoing challenges caused by the COVID-19 pandemic, such as labour shortages, supply chain disruptions, and increased competition have contributed to the need for manufacturers to innovate and optimise their manufacturing techniques and business practices.

A key focus for manufacturers should be ensuring supply chain resilience for bioprocess resins by sourcing multiple suppliers of key raw materials, securing domestic manufacturing capabilities, and manufacturing on multiple continents if necessary.

Downstream processing (DSP) techniques such as chromatography are used in monoclonal antibody (mAb) production to remove unwanted contaminants and to obtain a highly purified end product during purification. Manufacturers should aim to intensify their purification process by adopting processing methods that achieve sufficient speed, high throughput, and efficient use of facility space. As DSP plays a critical role in maintaining product safety, future-proofing is essential; this relies on robust supply chain networks.

It is crucial to choose products and suppliers with a proven track record in innovation to meet the ongoing demand for chromatography resins with high binding capacities and mitigate manufacturing bottlenecks in downstream purification. This way, manufacturers can ensure a bright future for mAb bioprocessing in the face of ongoing global uncertainty.

The Emergence of Novel Purification Methods

Novel antibody-based therapies are increasing in prevalence, reflected in the bispecific antibody market for cancer therapies, which is predicted to grow by over $400 million by 2027.[1] With the complexity of antibody-based therapies steadily increasing, classic purification methods may no longer be viable.

Chromatography resins made of cross-linked agarose, glass, or polymer beads bound to a Protein A ligand via a linker are commonly used in mAb purification. Protein A exhibits a strong affinity for antibody-based materials and can form a complex at pH levels ranging from 5 to 8, with the bound antibody being eluted when the pH is lowered to acidic conditions. This method is generally employed in the initial stages of development and maintained throughout commercial production.

Novel antibody-based therapies do not always share the same characteristics as mAbs. Therefore, innovative approaches to chromatography, such as alternative Protein A resins that allow for elution at higher pH levels, may be required to maintain high yields.

High pH technology resins also offer increased capacity for binding antibody-based products, allowing for increased productivity and reduced resin usage. This can result in cost savings, as less resin is required to achieve the desired yield of purified product.

However, sourcing and introducing new resins into pre-approved processes can be difficult as these technologies are not easily available and may not have off-the-shelf solutions.

The Need for Supply Partnerships with Novel Purification Methods

Robust supplier networks are integral in the biopharmaceutical industry, especially as demand for novel purification methods, such as high-pH technology for resins, is growing.

By working closely with suppliers and partners, drug developers and manufacturers can benefit from various advantages:

1. Access to a Reliable Supply

A robust supplier network ensures a reliable supply of resins and other materials required for the manufacturing process. Having multiple suppliers in different geographic locations and with varying manufacturing capabilities can reduce the risk of supply chain disruptions due to unforeseen circumstances, such as natural disasters, pandemics, or regulatory changes.

2. Access to the Latest Purification Technologies

Working alongside established suppliers can open access to the latest purification technologies, improving the efficiency

and effectiveness of the purification process. With a partnership that provides expertise and trouble-shooting capabilities, manufacturers can produce higher-quality products faster, which will ultimately benefit patients.

3. Creating Cost Savings

As profitability is becoming paramount, a robust supplier network can also help manufacturers negotiate better prices for materials and services, which can result in cost savings for the company. This can ultimately lead to more competitive pricing for the product, which can benefit patients and increase market share.

4. Maintaining Thorough Quality Control

Working with a supplier that has a rigorous quality control program can ensure that the resins used in the manufacturing process meet the required quality standards. Patient safety is imperative within the biopharma industry, and ensuring product quality is high – without any impurities or contaminants – is a key advantage of having a robust supplier network.

Exploring Off-the-shelf Resin Options and Their Advantages

A robust supply chain helps to secure the immediate supply of off-the-shelf resins, which provide several advantages over custom-made resins. First and foremost, they are readily available, eliminating the need for long lead times and custom orders that can delay production timelines. This is especially important in the rapidly evolving biopharmaceutical industry, where time-to-market is critical.

In addition to availability, off-the-shelf resins offer the advantage of cost-effectiveness, as they are often less expensive than custom-made resins. They also offer consistent performance from batch to batch, ensuring the reproducibility of DSP.

However, a standardised approach for implementing off-the-shelf resins and innovative resin technologies into pre-approved processes is currently lacking, and regulatory approval is required before switching to alternatives.

Overcoming Regulatory Barriers when Implementing Alternative Solutions

The lack of a standardised approach for implementing a new resin into a pre-approved process is a significant challenge for the biopharmaceutical industry. This has prompted the sector to come up with a regulatory-recognised solution for implementing materials from an alternative supplier or source founded on a QbD approach.

The BioPhorum guidelines suggest that a detailed documentation approach to critical material attributes (CMAs) enables interchangeability, making manufacturing integration and regulatory approval easier. To ensure consistent product quality and safety, certain controls are required, such as testing specific attributes of Protein A by the supplier, verifying the viral control strategy, and assessing DSP capacity to remove unwanted materials.

The BioPhorum convention of defining a material by its function and CMAs could allow materials to undergo an equivalency investigation instead of manufacturing revalidation, as defined in the four-step process aligned with the latest International Council for Harmonisation (ICH) guidelines:

1. Outlining the characteristics of the raw material to ensure the quality and safety of the drug product.
2. Definition of the attributes of the raw material, such as chemical, physical, microbial, and other safety aspects.
3. Creation of a summary control strategy based on the knowledge of current products and processes to ensure quality and performance.
4. Combination of the information from the previous steps to define the CMAs.

By following these QbD steps, as recommended by BioPhorum, supplier flexibility is increased, and it could facilitate regulatory approval processes. This is particularly beneficial when sourcing pH-sensitive products.

Looking Toward the Future

As increasing numbers of novel antibody-based therapies enter the pipeline, there is a need for applying innovative technologies, a robust supply chain, and a way to incorporate these technologies into existing processes compliantly. Access to alternative purification materials is crucial for delivering new antibody therapeutics, and a QbD-led approach is essential to incorporate these materials into DSP.

As more manufacturers become aware of the benefits of innovative resin technologies, adoption is likely to increase, further reinforcing the need for suppliers to continuously expand production capabilities globally.

The BioPhorum guidelines provide a regulatory-approved process for implementing alternative purification materials, enabling interchangeability, and making regulatory approval easier. A supportive supplier partnership will also be essential as these technologies increase in demand and will help to ensure consistent product quality and safety for patients.

REFERENCE

1. https://www.globenewswire.com/en/news-release/2023/03/15/2627505/28124/en/Global-Bispecific-Antibodies-for-Cancer-Market-Report-2023-2027-Increasing-Prevalence-of-Cancer-Advantages-of-Bispecific-Antibodies-Over-Monoclonal-Antibodies-and-Strong-Pipeline-D.html

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