

Cell culture

# The drive for quality

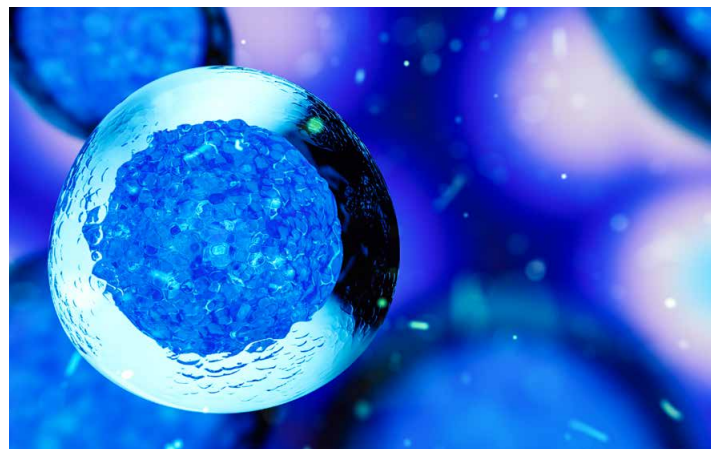
## Aiming for success in early mAb process development and beyond

To successfully develop and commercialize a monoclonal antibody (mAb), your product and process must comply with stringent quality regulations. The key to efficiently achieving this is to build on a solid foundation. A quality by design (QbD) approach aims to embed quality at every possible stage from the start. By implementing this proactive strategy, you can minimize variability and achieve higher consistency throughout, helping you master your quality goals and stay on course for long-term success.

When considering quality in mAb manufacturing workflows, the cell culture media and feeds used are critical, as they contain the necessary components—including carbohydrates, vitamins, amino acids, minerals, growth factors, and hormones—to support optimal cell growth, viability, and functioning. Healthy and

viable cells, in turn, help to maximize process performance through greater consistency and productivity.

For developers in the very early stages of mAb development, the benefits of considering how to proactively build quality into their processes are clear. With the importance of the cell culture media as a foundational element for success, this means choosing a supplier that can deliver consistency, quality, and reliability.

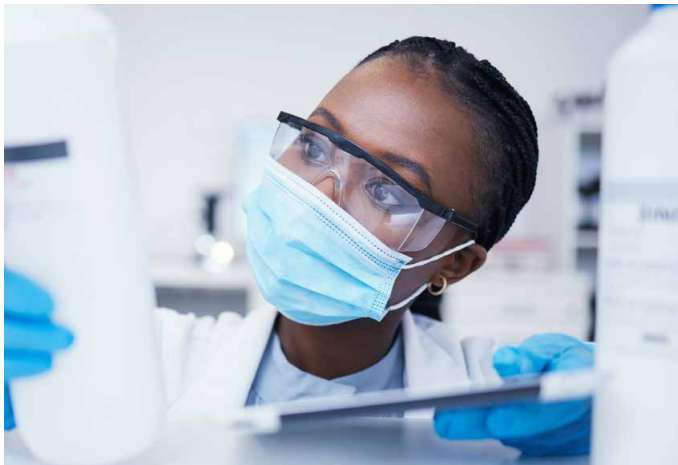


## The importance of consistency

With the central role that the cell culture media plays, reducing unwanted variability is essential. At smaller scales, variability can be more difficult to identify, but as processes are scaled up to commercial production volumes, unwanted variability can start to have a greater impact on performance. This can potentially lead to inconsistent product titers and suboptimal critical quality attributes.

Having a reliable supply of cell culture media is also important, as supply issues during development can delay progress and extend timelines. Developers may need to switch to a new supplier, which could require revalidation or formulation changes.

Ultimately, inconsistent media quality and supply can add unnecessary cost and complexity, harming process sustainability and economic feasibility. These difficulties can be compounded by the additional volume and quality requirements of scale-up, making the transition to commercialization more challenging.



## Where does media variability come from?

Reducing variability is clearly important, but developers first need to understand where it can be introduced. One potential source can be the presence of trace elements in the raw materials used to manufacture cell culture media. These trace elements, such as iron, zinc, manganese, and copper, are typically included in formulations due to their requirement in cellular processes. In desired concentration ranges, trace elements can positively impact cellular growth and quality attributes such as glycosylation, leading to improved biotherapeutic efficacy.

However, challenges can arise when trace elements are unknowingly introduced as impurities within raw materials and,

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as a result, their concentrations move outside of acceptable bounds. Some level of trace element variation is normal and expected, but too much can negatively impact media performance, resulting in lower protein yields and inconsistent quality attributes.

By taking a proactive QbD-driven approach, it is possible to implement mitigation plans and reduce the risk of impurities being introduced. When validating a media supplier, developers should look for strict sourcing protocols and robust, traceable supply chains. Some media suppliers may also have dedicated programs that conduct in-depth raw material characterization, allowing them to understand and proactively monitor particular raw material families and trace elements of interest. Using these data, they can conduct risk assessments to see how variability can be managed, helping them develop long-term risk mitigation strategies.

Variability can also be introduced during the media manufacturing process itself. Media production is a complex process, involving hundreds of incoming raw materials and numerous workflow steps. Manufacturers must employ rigorous quality control measures within their networks, as well as demonstrate comparability across the entire supply chain, to make sure finished products are equivalent—regardless of where they were made.

Implementing these measures provides risk mitigation for supplying consistent products. For example, during the production of dry-format culture media, the milling and blending steps grind and mix powdered media to create a uniform

product. If facilities use equipment or processes that are not equivalent, the resulting media could be inconsistent and may not perform as expected in a customer's process.

Another issue could be contamination of animal origin-free (AOF) components with animal-origin (AO) material. AO components will typically undergo stringent sourcing protocols and in-depth characterization to make sure they are of high quality and will perform consistently. However, for customers that have developed processes without AO components, contamination could introduce undesirable variability and negatively impact process performance. A media supplier should implement proactive systems around contamination controls to reduce risk, as well as perform rigorous vetting of incoming raw materials.

### Mitigating risk with robust quality systems

Quality management systems are used by media suppliers to help ensure that facilities within their network are harmonized and equivalent. Following the principles of QbD, actions to support quality should be implemented at every possible stage—from incoming raw materials all the way to release of finished goods. Through this, media manufacturers can help ensure they are maintaining the same high product quality standards across the entire network.

When selecting and validating a media supplier, it is important for developers to have an awareness of quality management. First, all process equipment needs to be properly validated, with aligned standard operating procedures and validated test methods. Products must also be manufactured in fully accredited and certified facilities using CGMP processes and raw materials. As mentioned earlier, a media manufacturer should also have dedicated protocols to keep AO and AOF products separate.

### Securing your supply, now and into the future

Avoiding supply disruption is crucial for developers and manufacturers at all stages of production. During the early phases, this is essential to allow process development to be completed on schedule. Supply availability is also key during the later manufacturing phases, to prevent costly delays caused by production stoppages or, in the worst-case scenario, late-stage process amendment and requalification. As such, supply reliability and assurance should be a critical consideration as early as possible.

There are two main facets to supply reliability. The first is being confident that any incoming products will always be

consistent and of the same high quality. Of equal importance is knowing that the supply is fully scalable to meet future needs. As developers progress toward commercialization, they need to be confident that increased volume demands can be met by their chosen media supplier, and that the products will perform consistently at all scales.

Supply assurance is also vital, as disruptions can hinder crucial early development and validating alternative products from new suppliers can be costly. A media supplier should have redundant manufacturing capacity built into their network, with multiple qualified facilities available for use. This means that if there is a disruption at one facility, an equivalent product can be sourced from another. Some suppliers may have in-house demand planners that can work proactively with early-stage developers to forecast future requirements and help ensure their supply can be assured in the long term.

### Prioritizing quality from R&D to commercial production

A proactive, quality-led approach is of critical importance for developers in the early stages of process development, helping them to create a process that can be seamlessly transitioned to commercial production. A key foundational element of this approach is a scalable supply of high-quality cell culture media that can maximize process performance and consistency.

By working with a media supplier that has the principles of QbD at the heart of everything they do, developers can be confident in the consistency of their media quality and supply. To achieve this, developers should look for a supplier offering rigorous raw material sourcing, facility harmonization, product equivalency, and site-to-site manufacturing redundancy. These capabilities can help streamline the scale-up process and reduce the risk of challenges arising during the journey toward commercialization.



## **Achieve your process performance goals**

### **Master the course, stay on target**

Having access to high-quality and reliable cell culture media is crucial to the success of your process.

That's why we have an in-depth equivalency program that is implemented at all sites within our global cell culture manufacturing network.

The program includes but is not limited to: harmonized capabilities across raw material sourcing, equipment, manufacturing processes, and finished product testing, to deliver a scalable supply of consistent, high-quality products.

Furthermore, our global media manufacturing network has been designed to maximize supply assurance, providing manufacturing redundancy and minimizing the risk of delays.

Supported by our extensive range of Gibco™ Media by Design™ Services and experienced field application scientist (FAS) teams, we can work closely with you to achieve your process goals—now and into the future.

**Learn more about how our portfolio of scalable products and extensive technical support services can help you unlock your cell culture edge at [thermofisher.com/performance](https://thermofisher.com/performance)**

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