

Monoclonal antibody

Strategies to streamline biotherapeutic development

Biotherapeutic development relies on precise, reproducible and scalable workflows. Commercial solutions, like Applied Biosystems™ kits and integrated systems, simplify sample prep, assays and data analysis while reducing variability – helping to accelerate development and maintain regulatory compliance. Thermo Fisher Scientific's commitment to offering training and support helps laboratories achieve efficient, reliable workflows that enhance product quality, safety and consistency across all stages of biotherapeutic production.

Introduction

Quality is a foundation of biotherapeutic manufacturing. Whether monitoring product safety, product quality, product potency or supporting environmental monitoring, manufacturers are guided by quality standards to protect patient outcomes with today's advanced therapeutic medicines. However, the goalposts for quality assurance (QA) and quality control (QC) standards are constantly evolving, leading to difficulties in meeting regulatory compliance and optimizing processes. To address this, Thermo Fisher Scientific offers a portfolio of analytical solutions, designed to support workflows from sample prep through to data analysis (Figure 1). This facilitates standardization of key workflow components, helping users to maintain compliance, achieve consistency, and reduce data variability.

The role of analytics in biotherapeutic manufacturing

Bioproduction analytics play a critical role in helping to ensure the quality, safety, and efficacy of biotherapeutic products. A key aspect of this is sample preparation, as consistent sample preparation facilitates consistent assays, which in turn strengthens data reliability and confident conclusions.

Analytics underpin every stage of product development, from raw material testing and in-process checks to lot release. They can also support regulatory compliance across global markets by providing regulators with essential data on product identity, purity, process control, qualification, validation, and QA/QC.

For final products, analytics confirm stability, specifications, and inter-lot comparability while addressing safety concerns, such as contamination risks detected through microbial and mycobacterial testing. In some cases, contamination events may prompt facilities to develop in-house analytical assays to decrease remediation time and cost. However, developing sensitive, robust assays requires a significant investment of time, expertise, and resources. Standard operating procedures (SOPs) must be created for reagents and equipment, and validating new assays may add further resource demands.

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How to choose an analytical method

Choosing an analytical method for biotherapies requires balancing regulatory expectations, ease of implementation, and scalability. Regulatory agencies expect assays to be considered as early as Phase I trials, with methods that can expand alongside product development. As programs progress from treating a handful of patients to hundreds in later clinical phases, assays must be robust and scalable to help ensure consistent, reliable results throughout the product lifecycle.

Analytical methods can be developed in-house or commercially sourced. While commercial kits may have an upfront cost, the hidden expenses of in-house development, including time, resources, and regulatory adherence, are often overlooked. Some products require specifically customized assays, but for many others, commercially based assays can provide faster workflows, reduce the developmental burden, and support reproducibility.

The comprehensive offerings from Thermo Fisher Scientific, including the Applied Biosystems™ suite of commercial kits for analytical testing, feature assays for mycoplasma detection, bacterial and fungal detection and identification, and residual DNA viral quantification. These can help reduce implementation timelines, staffing needs, overhead costs, and expertise requirements across various applications. Furthermore, the portfolio targets specific workflow bottlenecks, such as complex microbial detection, contamination risks, and inconsistent assay results (Figure 1).

The Applied Biosystems™ MicroSEQ™ Microbial Identification System streamlines microbial detection using genetic sequencing, offering a fully optimized workflow that can reduce complexity and saves time. Sample preparation is simplified, eliminating the need for testing DNA concentration, and collection from bacterial or fungal organisms is efficient. This single system supports turnaround from sample to result within five hours.

The Applied Biosystems™ resDNASEQ™ Residual Host Cell or plasmid DNA kits help quantitate residual host cell DNA risks through a closed-tube system combined with automated workflows. DNA extraction via the Applied Biosystems™ PrepSEQ™ system and automated on Thermo Scientific™ KingFisher™ instruments, operates within deep-well plates to reduce cross-contamination. Probe-based qPCR assays provide high specificity for the target sequence, minimizing background signals and facilitating reliable results.

Applied Biosystems™ MycoSEQ™ Plus and ViralSEQ™ kits address in-process and lot release testing, adventitious and viral vector characterization for gene therapy applications.

The MycoSEQ Plus assay targets mycoplasma species detection, a key component of all regulatory lot release specifications. ViralSEQ kits can be used in detecting adventitious infections during lot release testing or quantitating viral particles from cell-based bioproduction systems with precision.

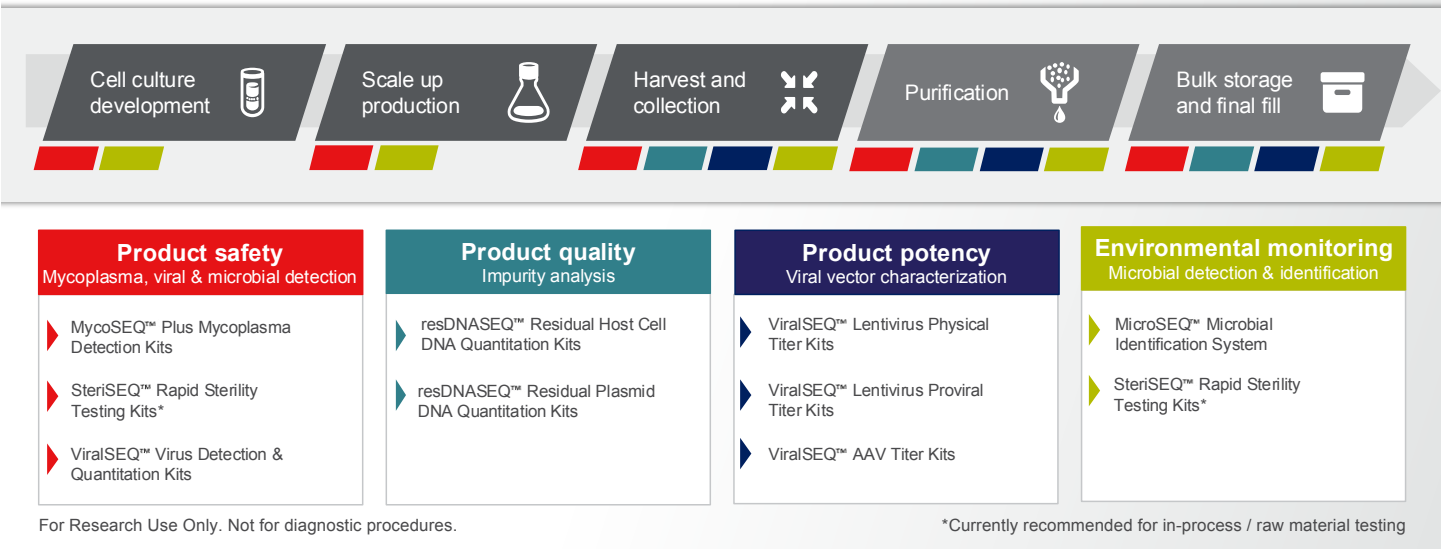


Figure 1. Commercial kits offered by Thermo Fisher Scientific for each stage of biotherapeutic development.

The advantages of fully integrated solutions

Adopting fully integrated solutions offers several key benefits, including consistent performance, reduced resource demands for assay development and optimization, as well as simplified procurement by reducing the need to qualify reagents from multiple vendors. These solutions also streamline the preparation and qualification of standards and controls. In addition, methods are supplied with the assays, reducing the burden of SOP development.

Beyond the assays, the accompanying services are built on years of global experience addressing multiple challenges, such as complex test samples, high cell counts, and short test turnaround time. Customers gain access to training programs that support rapid implementation and equipment qualification, as well as guidance throughout assay validation and troubleshooting process. Together, these features translate into significant savings in both time and stress.

While many sites initially attempt in-house assay development, issues such as qPCR inhibition, DNA contamination, and inconsistent results often drive the transition to commercial integrated solutions.

Integrating validated commercial solutions into biotherapeutic workflows

There is no set path for integrating commercial solutions into biotherapeutic workflows, as much of the transition depends on current facility equipment and management practices. Thermo Fisher Scientific offers field application specialists who visit the site to assess laboratory layout and current equipment and suggests the most suitable solution to enhance workflows (including equipment and software updates).

In monoclonal antibody production, environmental monitoring may be necessary to provide a holistic understanding of facility processes. This involves evaluating the total facility and its handling procedures to assess the bacterial and fungal environment and how these factors affect the growth of cells used to produce antibodies. When implementing solutions like the MicroSEQ ID System, it is essential to consider how this will integrate with existing operations. This includes evaluating expected improvements in performance and efficiency, the transition timeline, necessary personnel training, and the total duration of the integration process. Thermo Fisher offers trained specialists who navigate these considerations with customers.

Applications for monoclonal antibody workflows

Commercial solutions can assist in many aspects of monoclonal antibody workflows, including regulatory compliance, technology transfer, and reproducibility.

Regulatory authorities are familiar with Thermo Fisher solutions. For instance, the drug master file (DMF) for the Applied Biosystems™ MycoSEQ™ assay has been analyzed and logged with regulatory bodies for over a decade. When submitting their own regulatory filing, customers can reference the established regulatory history and documented information to help demonstrate lot-to-lot consistency and data to regulatory authorities.

Moreover, commercial solutions facilitate efficient technology transfer between development and manufacturing sites, particularly for monoclonal antibody workflows. Field application scientists collaborate with R&D labs to optimize assays, like residual DNA testing, accounting for variables such as cell types and inhibitors. The optimized protocol is then transferred to the QC lab, where these changes are implemented directly. This process eliminates additional optimization, significantly reducing the time and effort for technology transfer.

These solutions also reduce workflow variability by standardizing and automating key processes. Automation of sample prep and assay execution minimizes operator-dependent variability, supporting consistent results. Kits like the SteriSEQ assay help provide reliable sterility testing, reducing contamination, and supporting batch-to-batch reproducibility. By combining standardized protocols with automation, these solutions maintain high-quality standards, improve product consistency, and enhance overall efficiency.

Conclusion

Thermo Fisher recognizes the importance of laboratory efficiency. Tested, integrated solutions help streamline monoclonal antibody workflows, reduce variability, save time, and facilitate compliance. Automation and standardized protocols enhance reproducibility and ease technology transfer, while support guides implementation and troubleshooting. By simplifying processes and maintaining high-quality standards, these strategies help enable efficient, scalable, and reliable biotherapeutic production.