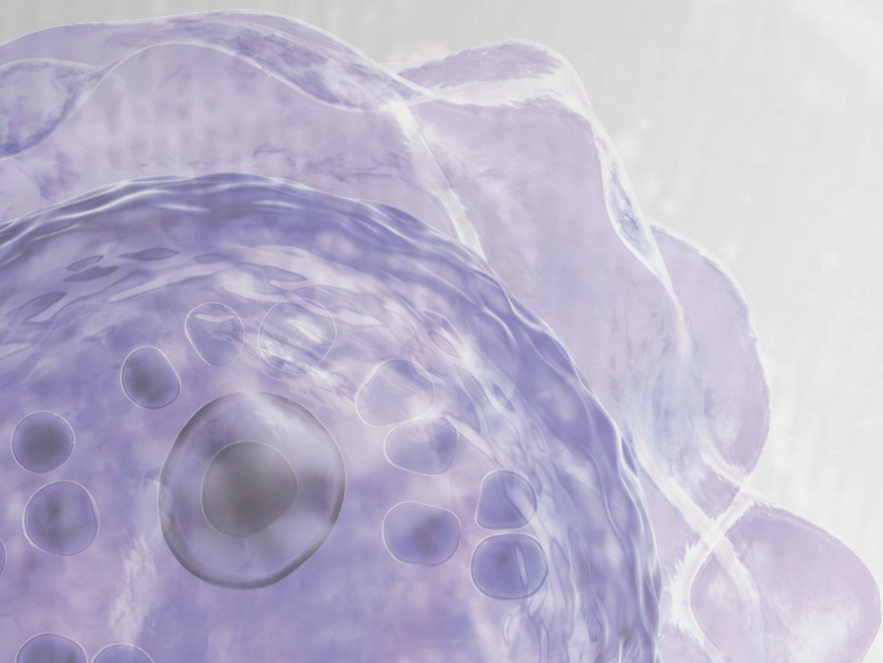


Cell and gene therapy

SUPPORTING SAFETY, QUALITY, AND EFFICACY

GMP LAB EQUIPMENT TO SUPPORT
UNIQUE QUALITY CONTROL STRATEGIES



THE IMPORTANCE OF QUALITY CONTROL FOR CELL AND GENE THERAPIES

Quality Control (QC) is a critical component of meeting Good Manufacturing Practices (GMP) regulatory requirements for advanced therapy medicinal products (ATMPs), including cell and gene therapies. Every batch of manufactured therapy must undergo complex evaluation protocols, in specially dedicated QC GMP facilities, to precisely determine the level of safety, quality, and efficacy of the final drug product. Due to the inherent variability of advanced therapeutics, including technologies and scientific approaches, standardization can be extremely challenging. QC activities for cell and gene therapies require extensive time, resources, and physical footprint. Quite often, the physical footprint of QC GMP facilities exceed the footprint of the cleanroom manufacturing process itself.

Therefore, reliable, fit-for-purpose laboratory equipment that supports reproducibility under GMP operation is paramount.

Since the QC methods can be very complex and sensitive, poor choices of laboratory equipment, reagents and consumables can contribute to low reproducibility and higher frequency of deviations. In the expectation to establish robust QC strategies, it is critical to employ adequate technology allowing for comprehensive coverage of all predetermined critical quality attributes (CQAs) that describe the therapeutic through advanced characterization. This characterization becomes the standard by which each subsequent batch will be evaluated before can be released for medicinal use. The process of testing these critical features is paramount to confirm the status of safety, quality, and efficacy of the final product. Robust characterization and QC strategy is a key to establishing trust with regulatory bodies and maximizing advance therapy success.

Reliable and fit-for-purpose laboratory equipment that offers clear data driven performance specifications can help streamline your QC strategy and support trust building with regulatory bodies. There is no place for errors since reproducibility is paramount for these time consuming, costly, and labor-intensive QC GMP methods. Our broad range of Thermo Scientific™ products are designed to support scientists and QC methods in a variety of QC GMP lab environments, including molecular biology, microbiology, analytical biochemistry, and cell biology.

Thermo Scientific™
Sorvall™ Legend™
Micro 17R
Centrifuge

Thermo Scientific™
TSX Series High-Performance
Undercounter Lab Refrigerator



QUALITY CONTROL ASSAYS MAY INVOLVE AN EXAMINATION OF:

SAFETY (PURITY AND STERILITY)

This refers to ensuring the absence of microbial and non-viable particulates. To maintain microbial sterility, cell and gene therapies are analyzed for bacterial, fungal, mycoplasma, and endotoxin contamination. Additionally, various forms of microscopic analysis are conducted to detect the presence of non-viable particulates that could potentially harm the patient. These analyses are typically developed and carried out in Good Manufacturing Practice (GMP) microbiology and molecular biology facilities.

QUALITY

This involves testing the identity, morphology, viability, and genomic stability. For gene therapies plasmid quantification and the assessment of viral vector for empty versus full capsid determination, may be critical. These variables are usually tested using methods developed and executed in GMP cell culture, biochemistry, and molecular biology suites.

EFFICACY

This is determined through tests designed to measure the therapeutic potency. The evaluation can be conducted in GMP cell culture facilities using specifically developed and validated potency or “kill” assays. For genetically modified cell therapies, the efficacy of the genetic modification must be tested. This is typically done using molecular biology techniques such as quantitative Polymerase Chain Reaction (qPCR).

The samples are taken at different stages of the manufacturing process and sent to different QC GMP labs for evaluation. The critical QC data generated must fit into predetermined acceptance criteria for each assay; even small deviations will require repetition of the test and if inconsistency occurs this can result in rejection of the full batch.



Pipetting in the **Thermo Scientific™ Herasafe™ 2030i** Biological Safety Cabinet



Thermo Scientific™ Solaris™ 4000 R Large Incubated and Refrigerated Benchtop Orbital Shaker



Thermo Scientific™ Heratherm™ IMP400 Refrigerated Incubator

MOLECULAR BIOLOGY

QUALITY CONTROL GMP LABORATORY

The molecular biology QC GMP facility will be equipped with a large array of specialised instrumentation including thermocyclers and next generation sequencing systems. But these complex methodologies could not be executed without fit-for-purpose general lab equipment including pipette systems, centrifuges, refrigerators, and freezers. These are the beating heart of every molecular biology lab and essential to sample preparation and storage, and, importantly, they can impact the reproducibility of the scientific data generated.

One important example of this is the centrifuge. Thermo Scientific™ General Purpose Pro Centrifuges—CTS™ Series are designed with reproducibility in mind. The accumulated centrifugal effect (ACE) function helps provide reproducible yields by automatically compensating for variations in acceleration through real-time centrifuge run time adjustments. This function helps ensure that all samples experience the same total centrifugal effect.



CRITICAL MOLECULAR BIOLOGY LAB PRODUCTS INCLUDE:

Thermo Scientific™ Products

- Aquanex™ Ultrapure Water Purification System
- FinnpiPETTE™ F1 Pipettes and Tips
- General Purpose Pro Centrifuges—CTS™ Series
- Herasafe™ 2030i Biological Safety Cabinet - CTS™ Series
- Heratherm™ Advanced Protocol Microbiological Incubators
- Microcentrifuges
- Nalgene™ Centrifuge Tubes
- Nunc™ Centrifuge Tubes
- Nunc™ Serological Pipettes
- Orion™ pH and Conductivity Meters, Electrodes, Solutions
- Solaris™ 4000 R Large Incubated and Refrigerated Benchtop Orbital Shaker
- Snap Cap Low Retention Microcentrifuge Tubes
- TDE Series Ultra-Low Temperature Freezers
- Vortex Mixers

Applied Biosystems™ Products

- MycoSEQ™ Mycoplasma Detection Kits
- QuantStudio™ 7 Pro Real-Time PCR System, 96-well, 0.2 mL
- resDNASEQ™ Human Residual DNA Quantitation Kits



CELL CULTURE

QUALITY CONTROL GMP LABORATORY

A dedicated GMP cell culture facility must be established to evaluate the identity, morphology, viability, and potency of a cell therapy. This facility houses specialised equipment including a microscope, an automated cell counter and a flow cytometry instrument. Quality laboratory equipment including a CO₂ incubator is important to maintain proper cell growth and health. A quality biological safety cabinet is critical to perform open cell manipulations and help maintain sterile conditions. A refrigerator and freezer will house critical reagents and media in precise conditions, and pipette systems, centrifuges, water baths, orbital shakers and pH meters are also critical to execute cell culture protocols and generate reliable data.

It is crucial that the conditions sustained in the CO₂ incubator chamber are uniform from top to bottom and side to side, so that all cells experience the same conditions. It is even more important that the incubator recovers quickly to desired conditions following every door opening. Donor-derived primary cells are extremely reactive and sensitive. Results from potency or kill assays can vary depending on the conditions under which these cells are cultured. Thermo Scientific™ Heracell™ Vios™ CR CO₂ Incubators – CTS™ series and Thermo Scientific™ Forma™ Steri-Cycle CR CO₂ Incubators – CTS™ series help ensure tight uniformity and recovery of all parameters within ten minutes, with proven contamination control methods to help achieve reproducible culturing conditions.



Heracell Vios CR
CO₂ Incubator - CTS Series

CELL BIOLOGY LAB PRODUCTS INCLUDE:

Thermo Scientific™ Products

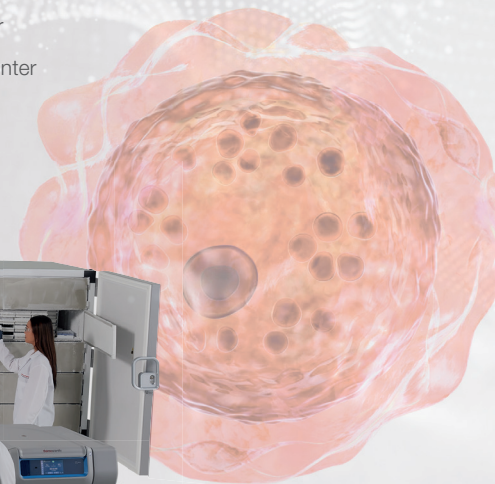
- Aquanex Ultrapure Water Purification System
- CO₂ Resistant Shaker
- Digital Rocker
- Finnpiquette F1 Pipettes and Tips
- General Purpose Pro Centrifuges - CTS Series
- Heracell™ Vios™ CR CO₂ Incubators - CTS Series
- Herasafe 2030i Biological Safety Cabinet - CTS Series
- Nalgene™ Centrifuge Tubes
- Nalgene™ Rapid-Flow™ Sterile Disposable Filter Units with PES Membranes
- Nunc™ Centrifuge Tubes
- Nunc™ EasYFlask™ Cell Culture Flasks
- Orion pH and Conductivity Meters, Electrodes, Solutions
- Precision™ Circulating Water Baths
- TDE Series Ultra-Low Temperature Freezers

Invitrogen™ Products

- Attune™ CytPix™ Flow Cytometer
- Countess™ 3 Automated Cell Counter
- EVOS™ M7000 Imaging System

Gibco™ Products

- Media

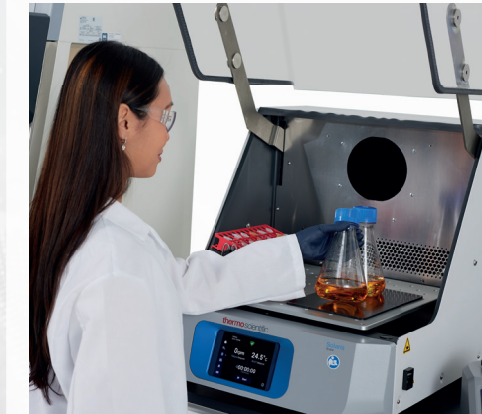


MICROBIOLOGY

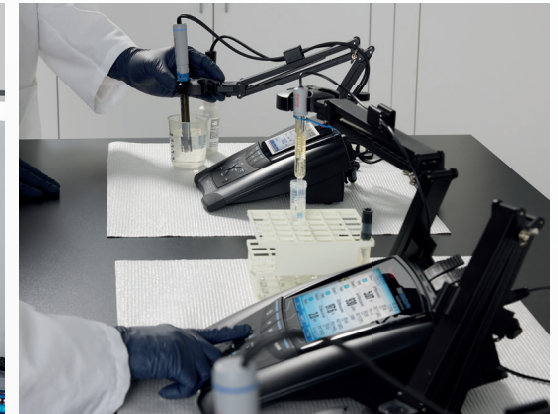
QUALITY CONTROL GMP LABORATORY

Evaluating product sterility plays a huge role in QC for advanced therapeutics, including cell and gene therapies. Due to the unique properties of live medicines, there are clear limitations for the final product sterilization. Therefore, a GMP microbiology lab can play essential role in evaluating the purity of the end product. There are a multitude of different assays needed to fully evaluate the final purity and safety.

Microbiological sterility is determined by a 14-day plate assay, a classical microbiology method which cannot be performed without a standard or refrigerated microbiological incubator designed for long-term incubation studies. Another GMP microbiology essential is a temperature-controlled shaker. Solaris Shakers are equipped with a durable, heavy-duty motor. This tri-balanced drive mechanism is maintenance free, designed to handle heavy, uneven loads and comes with an exceptional 10 year warranty to help you achieve reproducible performance for years to come.



Solaris 4000 R Large Incubated and Refrigerated Benchtop Orbital Shaker



Orion pH and Conductivity Meters, Electrodes, Solutions

INSTRUMENTS PRESENT IN A QC MICROBIOLOGY LAB INCLUDE:

Thermo Scientific™ Products

- Aquanex Ultrapure Water Purification System
- Finnpipette F1 Pipettes and Tips
- General Purpose Pro Centrifuges - CTS Series
- Heratherm™ Refrigerated Microbiological Incubator
- Heratherm™ Advanced Protocol Security Microbiological Incubator
- Heratherm™ Advanced Protocol Security Ovens
- Herasafe 2030i Biological Safety Cabinet - CTS Series
- Microcentrifuges
- Nalgene™ Biohazardous Waste Containers
- Nalgene™ Centrifuge Tubes
- Nunc Centrifuge Tubes
- Nunc Serological Pipettes
- Orion pH and Conductivity Meters, Electrodes, Solutions
- Snap Cap Low Retention Microcentrifuge Tubes
- Solaris 4000 R Large Incubated and Refrigerated Benchtop Orbital Shaker
- TSX™ Universal Series Ultra-low Temperature Freezers
- Vortex Mixers



ANALYTICAL BIOCHEMISTRY

QUALITY CONTROL GMP LABORATORY

An analytical chemistry lab is essential to any type of medicinal drug QC evaluation. For example, viral vectors — commonly used in cell and gene therapies— must be tested for full versus empty capsid ratios. Methodologies usually adapted here utilize ultra-high performance liquid chromatography (UHPLC) and mass spectrometry (MS) technologies. These QC facilities also require a full spectrum of lab equipment, including pipette systems, centrifuges, refrigerators, freezers, and high-quality water purification systems. The day-to-day operations with UHPLC- and MS-based methods require huge amounts of Type I and Type II purified water for sample and buffer preparation. A pH meter and associated products, plays a critical role in everyday GMP operations. Reliability and robustness are critical for both water purification and pH testing. A fit-for-purpose pH meter and water purification system will help to ensure your buffers are accurate and high quality.

Daily pH meter calibration is a critical activity in the GMP analytical lab. Employing the appropriate pH meter, electrode, calibration buffers, and maintenance solutions will help ensure that your calibrations will pass strict criteria and the readings will be quick, accurate, and reliable. Micro pH electrodes allow for testing of small volumes such as micro centrifuge tubes. Orion pH and Conductivity Meters are capable of logging thousands of data point sets with time/date stamps. Data is transferable via USB or RS232 cable to a printer or computer, to support 21 CFR Part 11 compliance for electronic data recording.



TSX Series High Performance Undercounter Lab Refrigerator



INSTRUMENTS USED IN AN ANALYTICAL CHEMISTRY GMP QC LAB INCLUDE:

Thermo Scientific™ Products

- Aquanex Ultrapure Water Purification System
- Finnpiquette F1 Pipettes and Tips
- Herasafe 2030i Biological Safety Cabinet - CTS Series
- Heratherm Advanced Protocol Security Ovens
- Microcentrifuges
- Nalgene Centrifuge Tubes
- Nunc Centrifuge Tubes
- Nunc Serological Pipettes
- Orion pH and Conductivity Meters, Electrodes, Solutions
- Snap Cap Low Retention Microcentrifuge Tubes
- Solaris 4000 R Large Incubated and Refrigerated Benchtop Orbital Shaker
- Sorvall X4 R Pro Centrifuges - CTS Series
- TSX Series High-Performance Undercounter Lab Refrigerators
- Vortex Mixers

ADDITIONAL RESOURCES

Find out more about laboratory products for cell and gene therapies thermofisher.com/cgtlabproducts

Experience our virtual tour: [Cell Therapy Interactive Lab](#)

Learn more about building and expanding your lab: thermofisher.com/newlab

Raising the bar on more sustainable product design thermofisher.com/greenerbydesign

Visit one of our Customer Experience Centers

- Maryland, United States
- Singapore
- Eindhoven, Netherlands

■ Find out more at thermofisher.com/cgtlabproducts

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