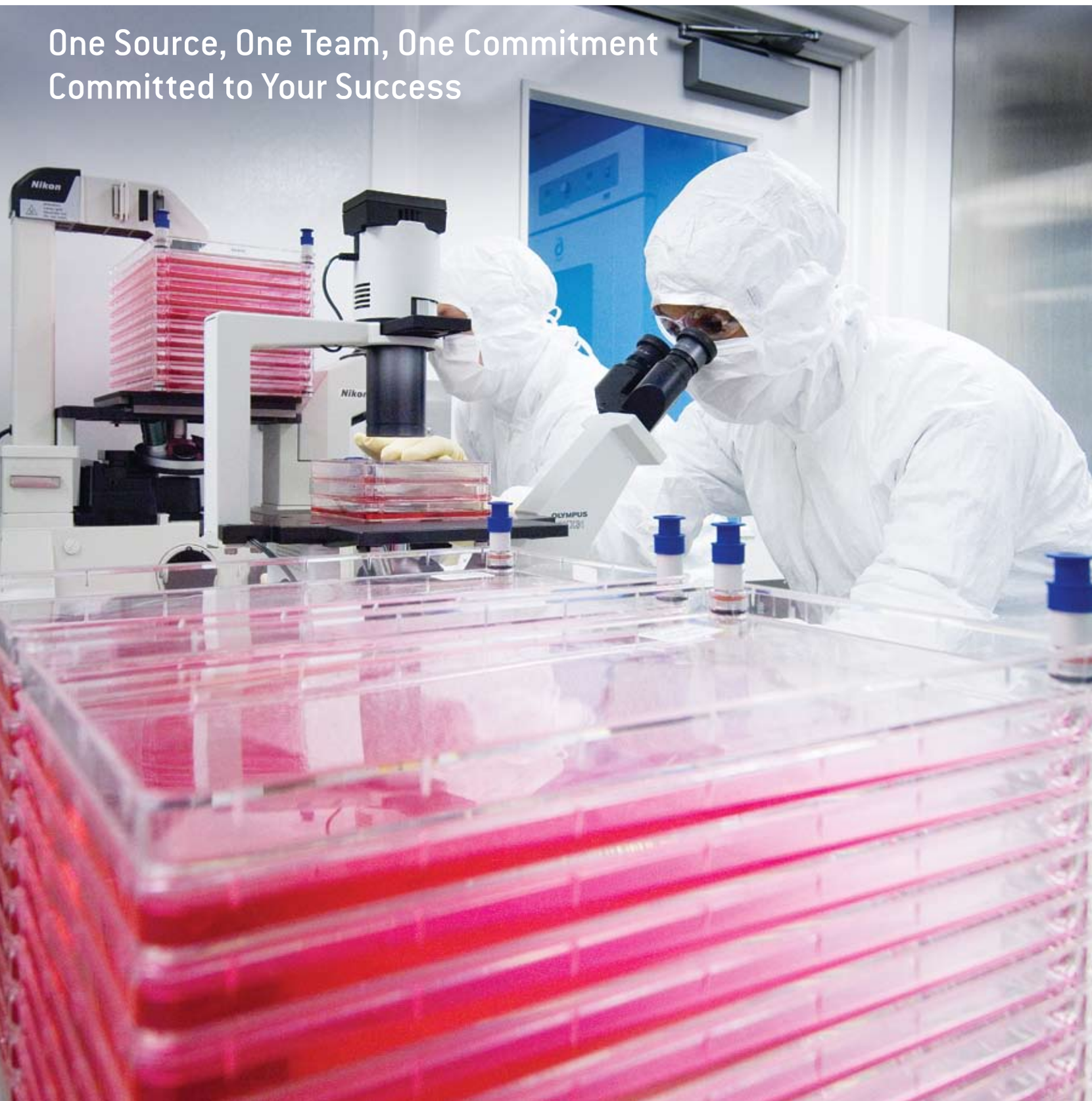
Lonza

Cell Therapy Capabilities



Process Development

Lonza has what it takes to transition from development to commercialization of your product. Prior to any development work, we open a dialogue with our clients to transfer information and verify existing methodologies, creating a defined baseline against which process improvements are easily measured. Our goals are simple: to ensure that all aspects of your process are optimized for maximum results and that there is a smooth transition to manufacturing and commercialization. From our expertise in process scale-up and design to media optimization, bioassay development and validation, and veterinary services, our staff is prepared to work with you and guide you every step of the way.

Tissue Acquisition

The Tissue Acquisition group obtains human tissue from many Tissue Recovery Agencies in the U.S. and manages its own living Donor Programs to provide unique tissue-derived cells for our customers. Essential to our acquisition process is a properly executed and documented informed consent. Lonza is registered with the FDA as a tissue bank and holds licenses in the states of New York and Maryland for tissue banking activities.

Isolation and Culture

For bioresearch and drug discovery applications, we offer more than a thousand products and services, including normal and differentiating human cells. Our state-of-the-art custom cell isolation laboratories are staffed with some of the world's best cell culture technicians.

It was a natural progression for us to isolate and culture cells under cGMP, and then to use those skills to assist our customers in meeting their goals. In fact, we thrive on transforming research-based cell cultures and processes into cGMP procedures. That includes all forms of cell culture optimization and scale-up, including animal cell isolations for pre-clinical modeling.

BioAssay Services

Our BioAssay Services team prides itself on its diverse capabilities. Our expert staff will develop, qualify, and validate a bioassay to assess measurements per GMP or GLP guidelines as required, including the following:

Cell-Based BioAssays

- Apoptosis
- Differentiation
- Proliferation
- Purity
- Cytotoxicity
- Cytokine induction
- Necrosis
- Neutralization

Biological Systems Analyzed

- Adipogenesis
- Angiogenesis
- Hematopoiesis
- Neurology
- Osteogenesis
- Immunology

Whether you need to transition a cell line-based assay to primary cells, develop a product potency assay, have an assay that requires qualification or validation, or need an existing validated bioassay transferred, let us combine the power of primary cells with our expertise in innovative bioassay development and performance to help you.

Media Development

No two cell types are alike. Since 1947, we have successfully developed media designed to culture different cell types. Over the years, we've learned what it takes to optimize the interaction between unique primary cells and their media. We can develop a media formulation designed precisely to your specifications in a variety of packaging and delivery configurations, including formulations that are serum-free and of non-animal origin.

We've done all of this for countless numbers of applications and customers, and we can do it for you, too.

Processes for Freezing, Packaging, and Shipping Final Product

Therapeutic products frequently require process development to optimize the freezing medium. Whether you want to reduce serum content, eliminate it altogether for a medium of non-animal origin, or completely define your medium, our team of experts can work with you to meet your goals. Beyond the medium itself, we can assist you in optimizing cell concentration in the final product, as well as in optimizing the vessel to contain your final product.

Additionally, we have the expertise to assist you in packaging and shipping your product. From validation of packaging to ensure optimal temperature control during shipping to our handling protocols and the speed with which we deliver your product to the end user, we strive to exceed the expectations of our customers. We offer you the option of shipping on wet ice or dry ice, or in liquid nitrogen dry shippers, and our relationships with couriers allow us to track your product shipment from the moment it leaves our door until it arrives safely in the hands of the recipient.

Regulatory and Compliance Advisory

Our experience in formulating regulatory strategies has made us familiar with the requirements of the various regulatory agencies. As we work to develop the processes and formulations you will require to transition to commercialization, we will advise you and provide you with the detailed information that may be needed for your regulatory filings.

Everything we do under Process Development is done with our full commitment to the success of our customers. We pride ourselves on solving the tough challenges, providing guidance to our customers throughout the optimization process, and ensuring a smooth transition to manufacturing and commercialization.

Veterinary Services

The Veterinary Services department includes a fully compliant laboratory animal program to support your *in vivo* testing requirements. We are AAALAC accredited, USDA registered and licensed, and hold a Public Health Assurance Statement.

How to Contact Us

Phone: 800-654-4452, ext. 2375 or 301-898-7025, ext. 2375
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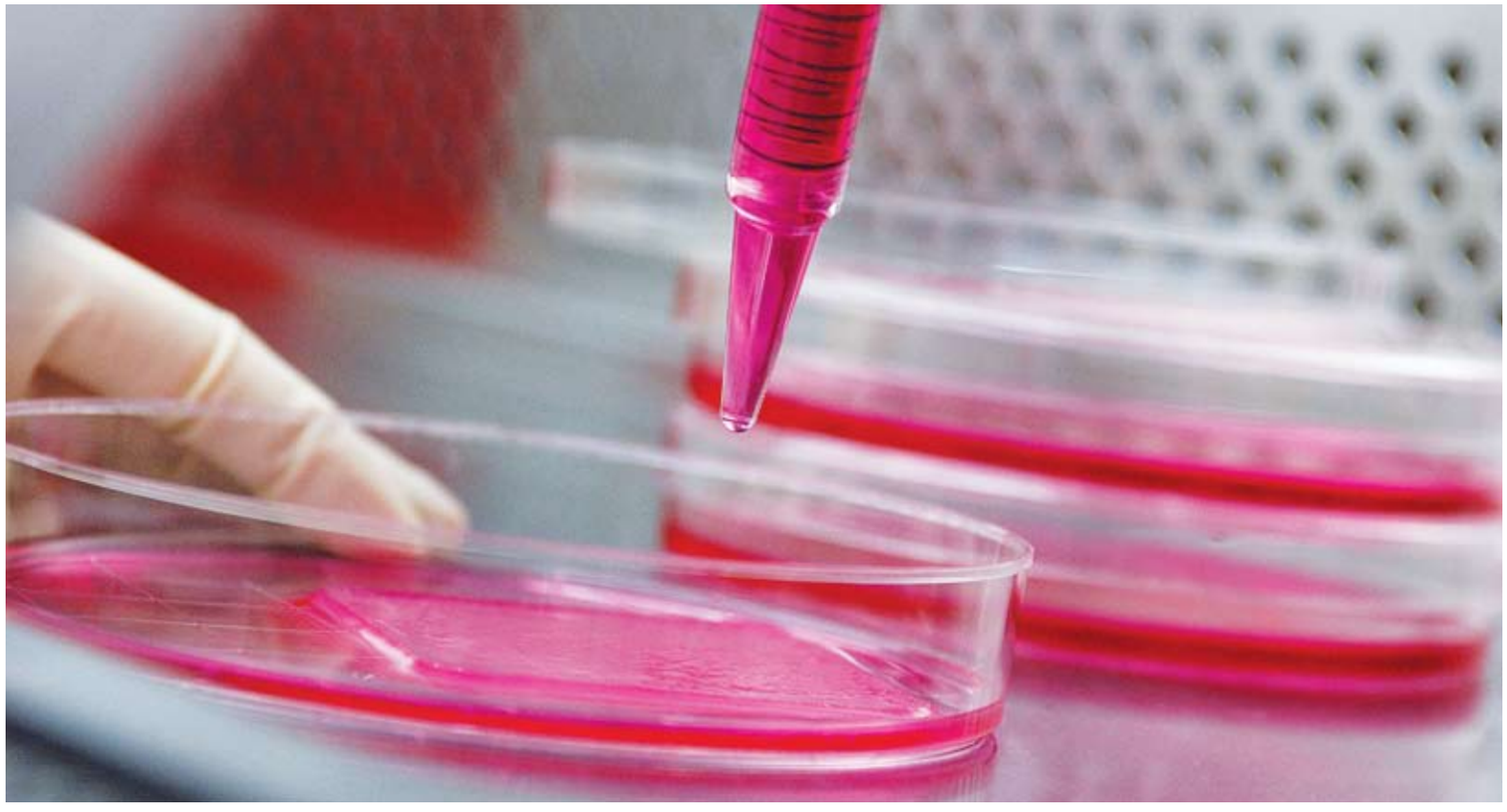
Cell Therapy Contract Manufacturing



Thanks to our more than 40 years of experience with normal human cells and exemplary cGMP compliance, Lonza is the global leader in development, manufacturing, and commercialization services for cell-based therapeutics. Utilizing the expertise and protocols devised in our Process Development organization, we partner with our clients to develop client-specific, custom protocols to meet each unique need, encompassing every aspect of the business from raw material requirements to final packaging and distribution. Open, consistent communications during the manufacturing process ensure optimal results and customer satisfaction.

We have extensive experience in acquiring tissues for FDA-approved therapeutics. Our staff ranges from the lead scientist who serves on the Standards Committee of the American Association of Tissue Banks (AATB) to physicians with in-depth expertise in donor testing and eligibility criteria and specialists who handle logistics, control, and documentation. Lonza will:

- Help clients comply with current donor eligibility criteria by developing the informed consent and health questionnaire specific to the tissue needed
- Develop client-specific programs for acquiring tissues, including acquisition process flow that suits the donor and tissue specifications
- Train tissue coordinators at participating sites
- Oversee donor selection and screening and the tissue acquisition process
- Determine final donor eligibility

Lonza works with organ and tissue procurement organizations, hospitals, and private physicians in the United States to collect tissues within the framework of the AATB standards and FDA regulations for manufacturing processes for clinical use. Lonza is also registered with the FDA as a tissue bank. Tell us what you need and we will employ our established, quality processes to obtain it for you.

Our state-of-the-art cGMP manufacturing facilities, located in the United States and in Europe, enable us to provide all the support services you might need to produce human cells for therapeutic use, including:

- Autologous cells of varying shelf life for shipment to the United States and Europe
- Allogeneic cells, including sourcing, production of cell banks, and expansion to product quantities
- Stem cell production via both master and feeder cell banks

Cell Therapy Contract Manufacturing

We are equipped for, and have experience with, flasks, roller bottles, beads, and cell factories, including tissue-engineered formats to meet specific customer requirements.

Our US-based suites currently comply with ISO Class 7 (Class 10,000) classification to meet US requirements, and we also offer a suite with ISO Class 5 (Class B) compliance for European needs. Our ISO Class 5 (Class B) suite meets all current European GMP regulatory standards. From the unidirectional flow design for materials and personnel to the equipment we utilize, the suites are engineered with exceptional quality in mind. Flexibility in design permits us to configure the suites to meet unique customer needs and optimize productivity. Each suite boasts a dedicated air-handling system, as well as a separate air-handling system for common areas, thus preventing cross-contamination. Additionally, every suite features its own dedicated cleaning and environmental monitoring equipment, as well as alarmed back-up equipment.

We are exceptionally aware of the need to segregate projects, and are fastidious about protecting your product, as well as your process. At the conclusion of each project, validated changeover and cleaning procedures are implemented, culminating in the Quality Assurance organization releasing the suite for use for each individual project. All of this translates to ensuring the integrity of your product and consistently meeting customer expectations with efficient systems and high quality results.

Lonza can take you through the entire life cycle of a product, from jump-starting clinical trials with cGMP-manufactured product to providing unrivaled commitment to large-scale production. Years of experience have culminated in extensive knowledge about what challenges lie along the path to commercialization. Talk to us about how we can help you successfully commercialize your product.

Regulatory and Compliance Services

Lonza has a wealth of expertise available to assist customers with the requirements of the FDA, EU, or other regulatory agencies. We can address your product labeling and document needs, prepare and approve all regulated documents prior to submission, or even interface with the regulatory agencies during audits. Our services also include writing the CMC section required for an IND, creation and submission of drug master files, and formatting and submission of the dossier.

Processes for Freezing, Packaging, and Shipping of Final Product

Therapeutic products frequently require process development to optimize the freezing medium. We will work with our team of Process Development experts in an effort to meet your goals, whether they are to reduce serum content, eliminate it altogether for a medium of non-animal origin, or completely define your medium. We can also help you to optimize cell concentration in the final product, as well as to optimize the vessel to contain your final product.

From validation of packaging to ensure optimal temperature control during shipping to our handling protocols and the speed with which we deliver your product to the end user, we strive to exceed the expectations of our customers. We offer you the option of shipping on wet ice, dry ice, or in liquid nitrogen dry shippers, and our relationships with couriers permit us to track your product shipment from the moment it leaves our door until it arrives safely in the hands of the recipient.

Distribution Services

Perhaps most importantly, getting your product into the hands of those who need it most is a critical goal. To that end, we provide clinical distribution services utilizing an experienced staff and infrastructure to eliminate extra steps and expedite the delivery of your product to the end user.

How to Contact Us

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Contact Information

Process Development

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Cell Therapy Contract Manufacturing

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Lonza Walkersville, Inc.
Walkersville, MD 21793

For further manufacturing or laboratory use.

BR-BSV-1 09/07

Lonza

Process Development

Cell Culture and Cell Systems

Many customers come to us with specific needs regarding cell cultures or cell systems. Our capabilities include, but are not limited to:

- Scale-up from flasks to large vessels
- Determining optimal cell seeding density
- Optimizing feeding schedules and cell densities
- Development of commercial-scale cryopreservation methods

Additionally, we have an expertise in isolating, culturing, and characterizing specific cell types from animals for pre-clinical *in vivo* models.

Media Development

Our many years of expertise in media development make us the perfect partner to optimize your media formulations. We start by growing your cells in over 80 different basal media in order to determine which formulations are optimal for your cells. Spent media from these cultures are analyzed to determine what components need to be rebalanced to obtain the best growth and cell function. Blending and supplementation experiments are performed, permitting us to determine the exact concentrations of individual components that are critical to optimal cell performance. Ultimately, we will formulate a medium that allows for the optimal balance of cell proliferation and function to meet your cell culture needs.

BioAssay Services

Bioassays are a critical part of the drug development pipeline, from discovery through clinical trials to lot release. The diverse skills of our BioAssay Services group make us an excellent partner, whatever your bioassay needs, whether for research and development purposes, or per cGMP or cGLP guidelines. We combine client-specific project management with rapid and flexible turnaround-time to meet your requirements.

BioAssay Services specializes in the development, qualification, and validation of cell-based bioassays. We apply the same world-class expertise used in development of more than a thousand cell culture products. No one knows more about cells than we do.

Our capabilities include, but are not limited to:

BioAssay Method Development

We have developed a wide range of bioassays to characterize biological and biopharmaceutical products. We will support you in the critical early phases of your bioassay's development with:

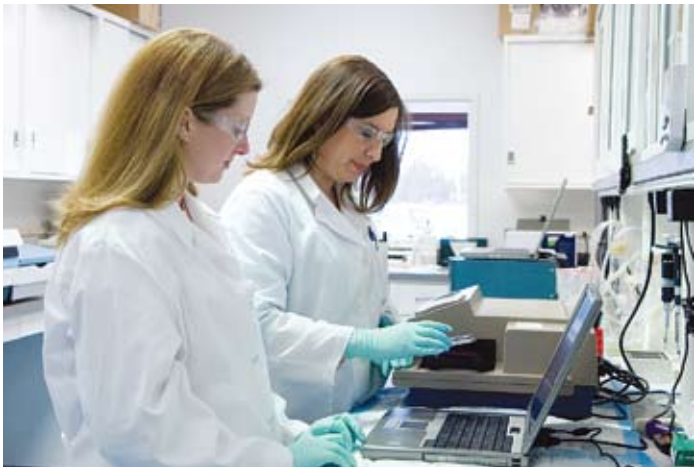
- Technology transfer
- Cell culture optimization
- Product range-finding
- Design of Experiment (DOE)
- Extension of the bioassay's working range
  - Drug development
- Increasing the bioassay's sensitivity
  - Drug purity
  - Drug formulation and stability studies
- Manufacture of cGMP master and working cell banks
- Report generation –comprehensive details of all procedures and results

BioAssay Qualification and Validation

We will qualify your bioassay and then validate the bioassay's parameters, including accuracy, precision, specificity, linearity and robustness, in accordance with regulatory guidelines.

BioAssay Performance

We perform validated stability-indicating bioassays and potency bioassays to meet your regulatory requirements.



Veterinary Services

Our skilled Veterinary Services staff can perform *in vivo* testing on a variety of species to meet your specific protocol requirements.

In addition to being an AAALAC accredited facility, we are USDA registered and licensed and hold a Public Health Assurances Statement.

How to Contact Us

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Lonza

Cell Therapy Contract Manufacturing

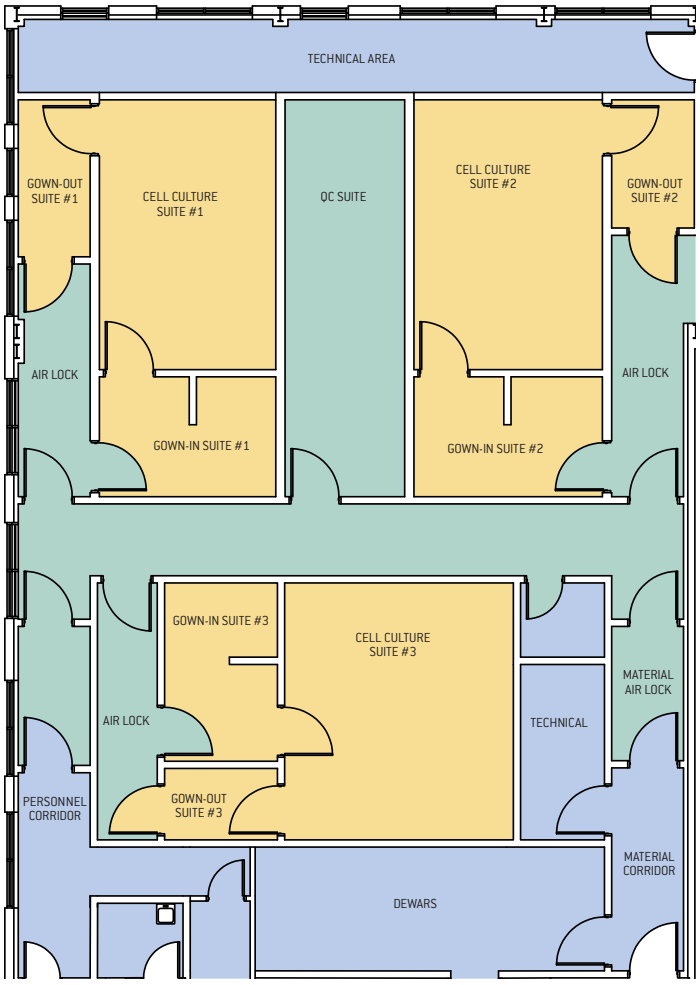
Lonza Walkersville, Inc. is a cGMP/GTP-compliant clinical cell processing facility, engineered with exceptional quality in mind and designed specifically to meet the needs of our cell therapy clients. The suites currently include ISO Class 7 (Class 10,000) to meet US requirements and ISO Class 5 (Class B) for European needs. Ranging in size from 275 to 1,000 square feet, they are designed with a flexibility that permits us to configure the suites to meet unique customer needs.

Facility Features

- Unidirectional flow design for materials and personnel
- Dedicated QC suite
- Redundant power systems
- Independent air handling systems
- Validated and remotely alarmed equipment
- Excellent technical and support staffs
- Adequate space for expansion into commercial production scale

This facility is an established FDA Registered Tissue Bank and is ISO 9001:2000 Registered.

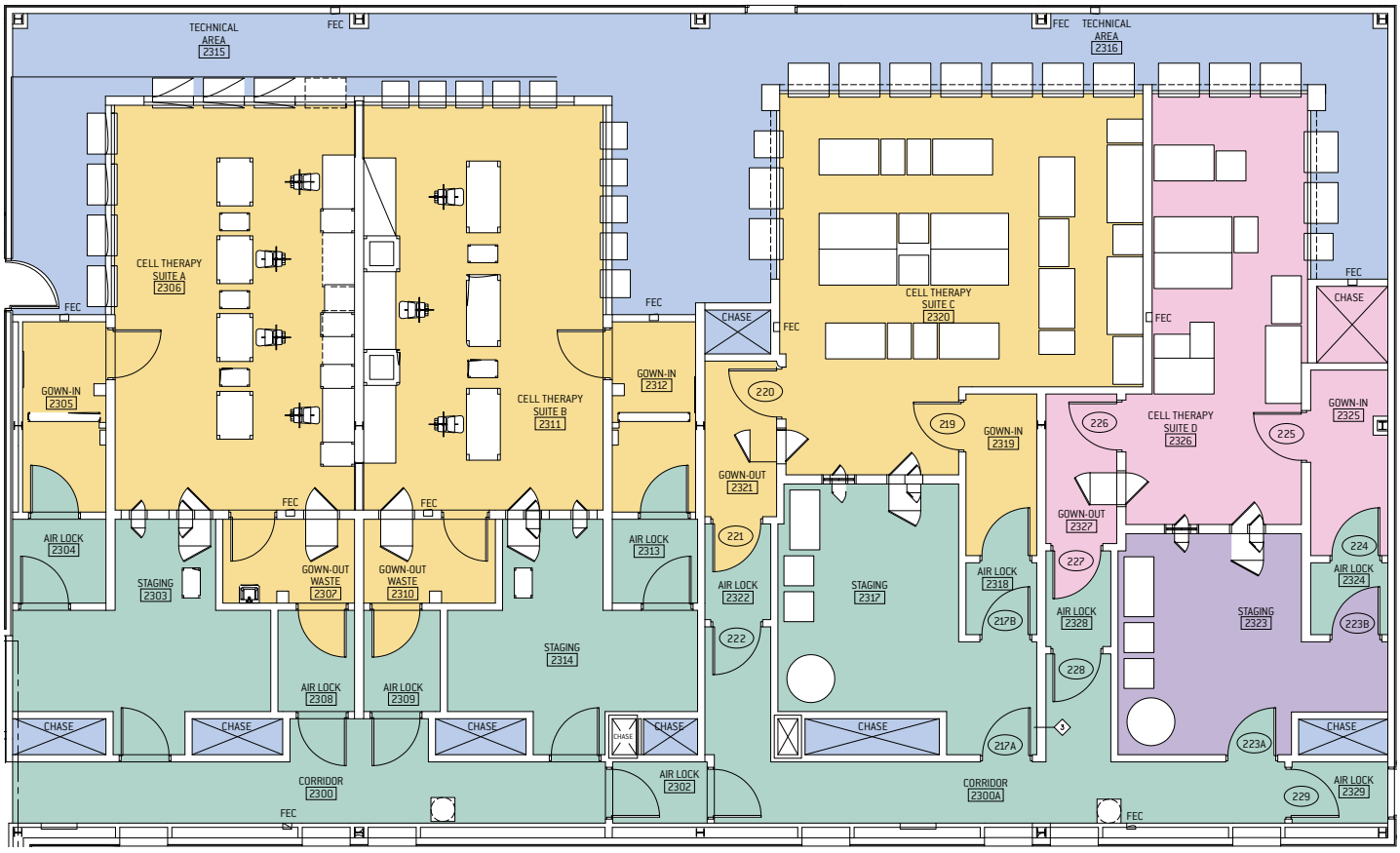
Walkersville Cell Therapy Suites I



Legend

- Class 10,000 area
- Class 100,000 area
- Unclassified area

Walkersville Cell Therapy Suites II



We also have a state-of-the-art clinical cell processing facility in Verviers, Belgium. Both EU and cGMP compliant, it has been inspected and approved by the Belgium Ministry of Health for cell therapy manufacturing, and is FDA registered.

Facility Features

- Unidirectional flow of materials and personnel
- Around-the-clock environmental monitoring
- Validated and remotely alarmed equipment
- Dedicated QC suite
- Multiple walk-in incubator rooms
- Space for expansion to commercial-scale production

Legend

- Class 10,000 area
- Class 100,000 area
- Unclassified area
- Class B
- Class D

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