ISOCell PRO

BIOAIR®

Advanced Therapy Isolator

EVERYTHING YOU NEED FOR CELL AND GENE THERAPY PRODUCTS AT YOUR HAND

Producing advanced therapy medicinal products (ATMPs) for therapeutic purposes is a complex task, for which aseptic conditions are only one part of the requirement. Apart from the clean room zone itself, you need trained operators and strict procedures to prepare the room and the people involved to be ready for the process. This requires huge efforts in terms of infrastructures, personnel training and compliance.

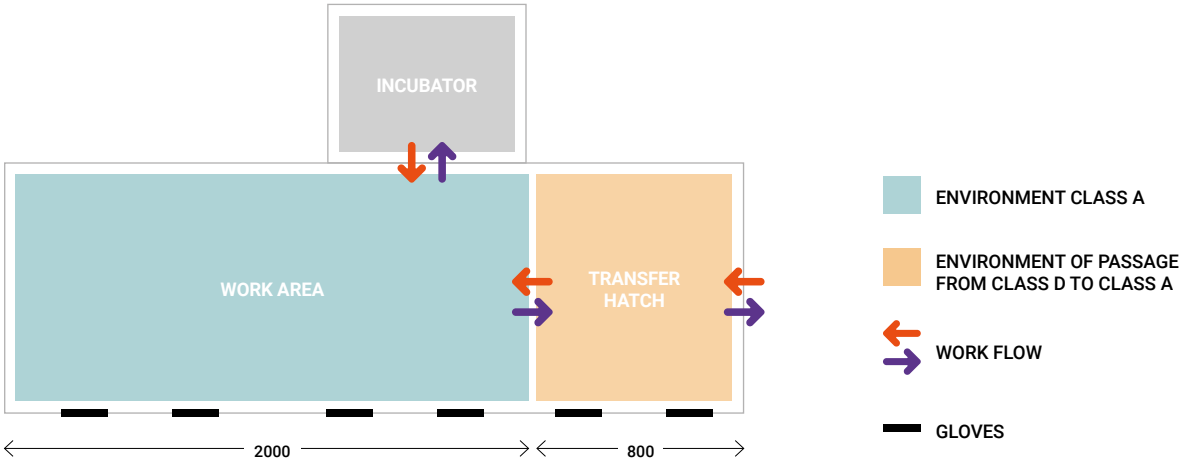
This approach is required by a wide range of advanced therapeutical approaches, including:

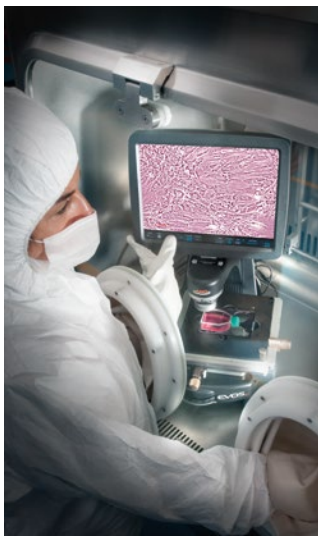
- Production of ATMPs
- Cell Therapy
- Gene Therapy
- Tissue engineering Therapy
- Regenerative Medicine

Bioair, with its ISOCell PRO Cell Therapy Isolator, can be the answer to your needs by providing a streamlined workflow environment reducing the set up and running costs of cell therapy products preparation while still operating within the restrictive confines of various regulatory bodies (FDA, EUP, USP) and industry guidelines (GMP, PDA).

- Simplicity of the ISO 5 location and easy gowning for most applications since isolator systems dedicated to cell production may be located in a Class D room with restricted access;
- Security with validated sterility of the working area and cross-protection of product/operator/environment.
- Traceability for all the steps of the sterile handling process.
- The initial sterility is provided by a dedicated H_2O_2 vapor (HPV) program to bio-decontaminate the work area and the material access area
- The sterility is maintained with the positive pressure of HEPA-filtered air. The outlet HEPA prevents against any return of non-sterile air.
- System is designed to be used in validated GMP processes

In 2015 SwissMedic issued the certificate of GMP compliance for a process at the Centre de Production Cellulaire (CHUV-Lausanne) where six ISOCell PRO units are installed. By achieving this goal Bioair's ISOCell PRO has become the first isolator recognized as part of a fully validated process to produce artificial tissues to be used in human therapy.





COST-EFFECTIVE SOLUTION

Infrastructural cost reduction:
Only Class D surrounding environment required
Reduction of the central air conditioning system
No need for specific consumables

Time reduction:
Faster Qualification/Validation
Decrease in process time (no need for operator to progressively pass from a class D to a class A, no need for specific clothes)
Decrease of decontamination time (H_2O_2 vapour)

Safest:
Smaller environment allowing easier monitoring and control
Increase of the stability of the environmental parameters in the working area
Possibility to install different units in a same room (independent alternative working area in case of problem).

UNIDIRECTIONAL AIRFLOW

The main working area is classified as class A according to GMP/EU, the aeraulics are designed to provide a unidirectional flow within both the main working area and the transfer hatch. The airflow in the transfer hatch is designed to increase during the opening of the product inlet in order to keep the internal environment clean and allow for a fast recovery of the class A environment.

INTEGRATED CO_2/O_2 INCUBATOR

The incubator is a custom device designed to fit into an isolator environment and connected to the SCADA system in order to monitor all the controlled parameters.

- Full access from the working area
- No need for transportation of samples in/out of the Class A environment during the procedures
- Sterilization of the incubator with hydrogen peroxide vapours

INTEGRATED MICROSCOPE

A microscope is included in the working area to allow fast and easy observation of the cell and tissue sample without the need to leave the clean area.

- 15" LCD monitor for real-time observation of samples
- Ethernet connection: all images are saved in a network location for later access
- SCADA interoperability: all images are viewable via the integrated PC panel

INTEGRATED WASTE SYSTEM

The bin is placed below the isolator and has an opening port inside the working area between incubator and microscope. The waste bin port is a rapid transfer port that allows to disconnect the bin only if the port is closed and allows to re-connect a sterile bin without loosing the sterility both of the isolator and of the bin's internal volume.

STERILIZATION

In order to guarantee a sterile environment, the ISOCell PRO is designed to allow sterilization with hydrogen peroxide vaporisation.
The sterilization can be made for the whole isolator (transfer hatch and working area at the same time) or for the transfer hatch only. This allows to quickly sterilize materials before introduction in the working area, reducing reagent consumption and avoiding interruption of the workflow.

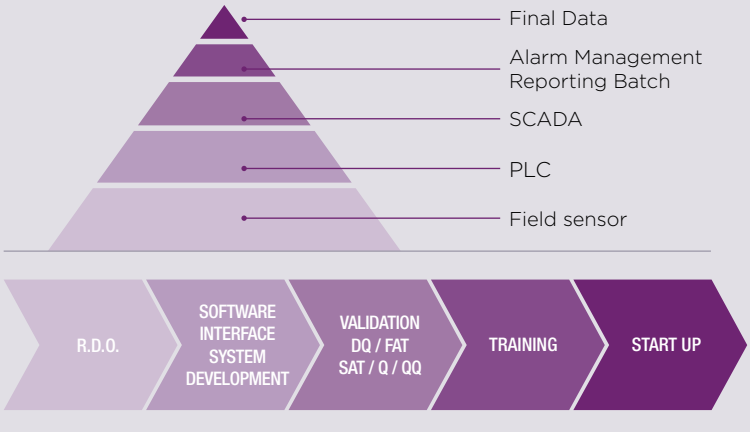
- Compatible with stand alone generator with an H_2O_2 outlet and a return inlet from isolator using integrated cam-lock connectors
- Data connection with the H_2O_2 vapour generator to allow full control of the process via the ISOCell PRO main interface
- Cycle data are recorded and the process is fully validable
- Pressure checks to ensure leak-tightness and avoid overpressures
- Auto-check to prevent issues before and during the sterilization cycle, with constant monitoring of all critical parameters

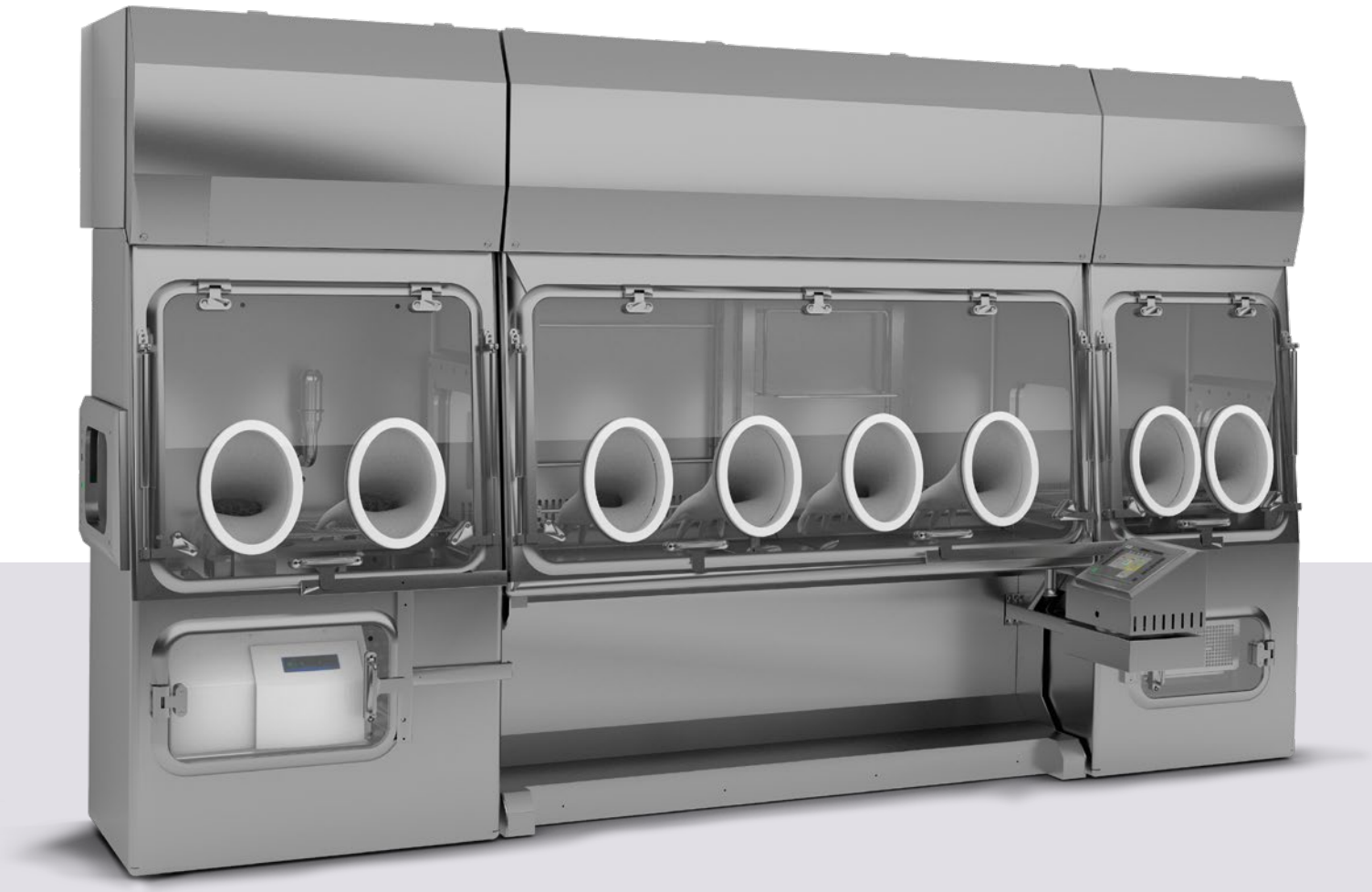
TRACEABILITY

Important parameters are monitored and may be recorded: the ISOCell PRO has an integrated Supervisory Control And Data Acquisition (SCADA) managing system that complies with the GAMP requirement and 21 CFR part 11 about data registration.

The FMS software Annex-1 is an application designed and built for the management and production of reports concerning the control of particulate contamination present in clean room production in the pharmaceutical industry.

- The process is always controlled by the operator.
- Security for both the operator and the process.

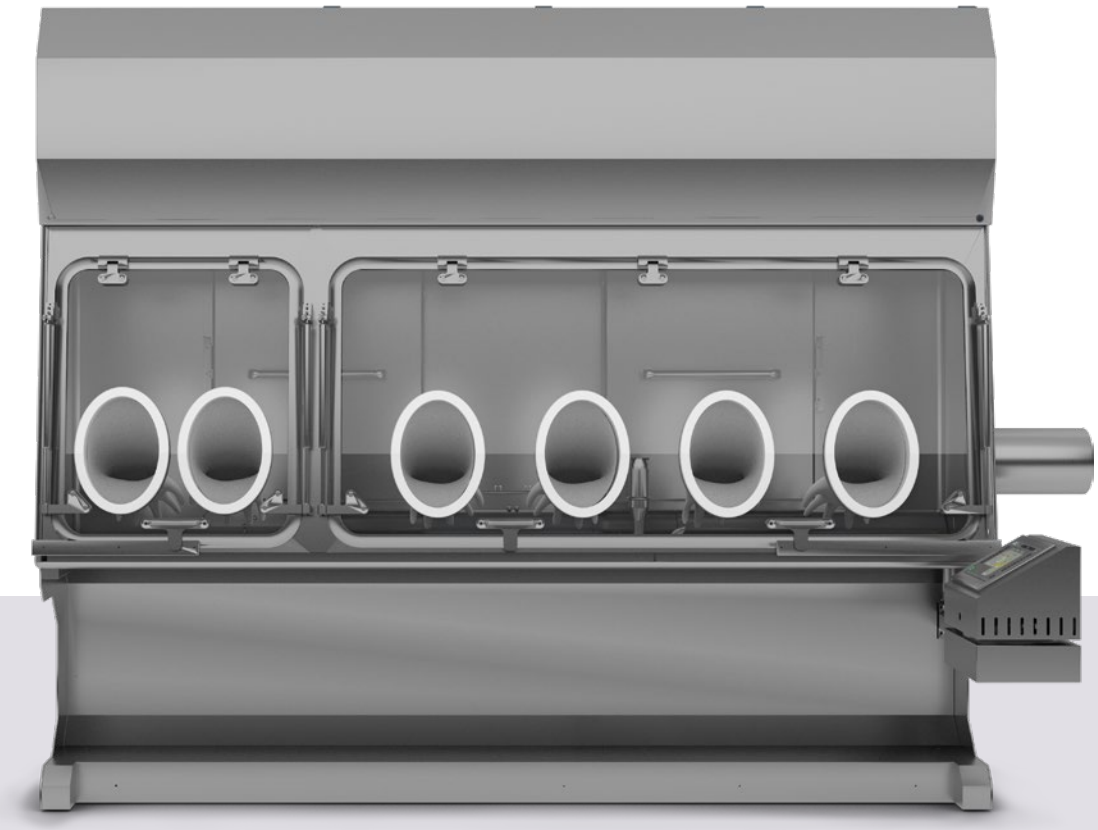




ISOCell PRO | CENTRIFUGE

In several processes producing advanced therapy medications, using a centrifuge is essential. The centrifuge, over the counter or refrigerated, will be selected based on your production needs and placed under the working space thus keeping the class A manipulation area free.

As for the incubator, it is fundamental that the centrifuge is used in compliance with the GMP rules that require to work in a controlled and monitored environment. Bioair proposes the ISOCell PRO centrifuge to meet this need.



ISOCell PRO | CO_2

Producing a wide range or advanced therapy medications requests large production spaces, particularly for the medications dedicated to expanding cells in incubator. The two incubators equipped with CO_2 and N_2 allow to work also in hypoxia.

The disinfection of the working area using hydrogen peroxide is effected without removing the cell coltures inside each incubator. These and other features make the incubator extremely flexible and able to meet a great number of processes' needs complying with the GMP.

ISOCell PRO

The manipulation incubator for the preparation of cell/genic therapy includes two stations, a microscope for the evaluation of the cell coltures status and an incubator for the storage and growth of the cell coltures. Furthermore, the ISOCell PRO can work in positive or negative pressure based on the processes of production to be implemented.

ISOCell PRO is the unique one on the market already installed, validated and currently used in a laboratory credited for productions in GMP of injectable cells (CPC-CHUV Lausanne, Switwerland).

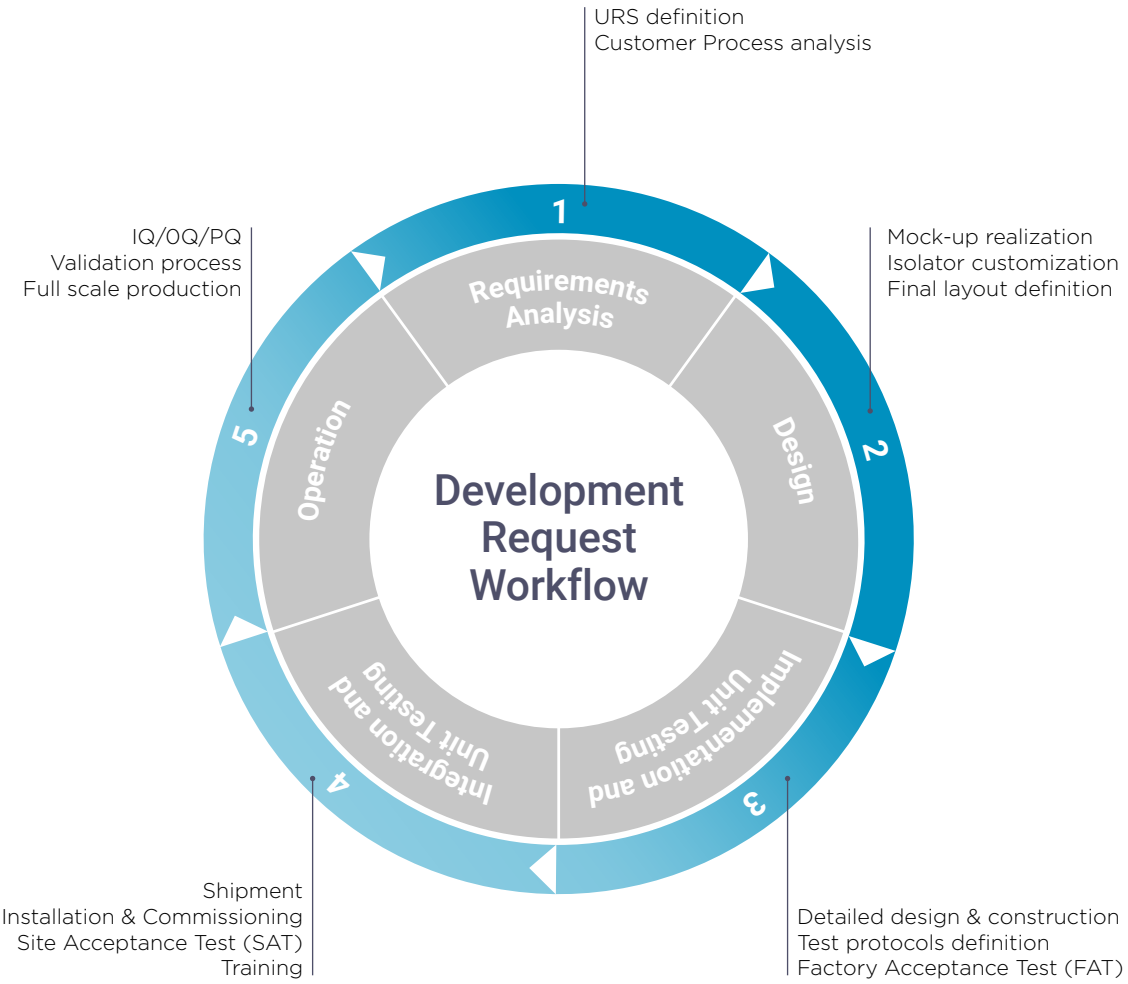
YOUR PROJECT, OUR SOLUTIONS

Bioair and its partners can provide a complete support for your project and requirements.

We believe that assisting the customer from the planning phase through the realization of mock-ups, the identification of technical solutions to meet process requirements, the installation and training, until the final steps of validation and follow-up, is the key for a successful project.

We have established a network of professionals who can help you integrate your process with the ISOCell PRO technology via customization and support, in order to achieve the best results in the most reliable and effective way.

For us ISOCell PRO is more than a product: it's a Project! Don't be just a customer: we are Partners, working togheter towards a common goal!



TECHNICAL SPECIFICATIONS

ISOCell PRO is realised in compliance with the Rules Governing Medicinal Products in the European Union (EudraLex) – Volume 4 EU Guidelines of Good Manufacturing Practice – Annex 1 Manufacture of Sterile Medicinal Products – 2008 revision.
In particular it is designed in accordance with the requirement for Isolator Technology (paragraph 21 – 25).

ISOCell PRO complies with the following European Directives and is designed according to the following European Norms:

- Machinery Directive 2006/42/CE
- EMC Directive 2004/108/CE
- ISO14644.1 – Cleanroom and associated controlled environment – Classification of air cleanliness
- ISO14644.7 - Cleanroom and associated controlled environment – Separative devices
- EN 61010:2010 - Safety requirements for electrical equipment for measurement, control, and laboratory use
- EC GMP guidelines: Rules governing Medicinal Products in the European
- Community, Volume 4, Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use
- Code of Federal Regulation (CFR) Title 21, Part 11

MAIN SPECIFICATIONS

Characteristic	Specification
Weight of the entire module (kg)	1500
External dimensions of the module (mm):	Depth: 1500 - Width: 2900 - Height: 2350
Total noise level of the module (in dB)	<55 dbA
Material used for the exterior construction of the module	Stainless steel AISI 304
Material used for interior construction of the module	Stainless steel AISI 304
Air cleanliness class inside the module	Environment of class A according to GMP EU / Vol 4 Annex 1 ISO 4.5 inside of the module according to EN ISO 14644.1
Working area average luminosity	>750 Lux
Air tightness of isolator	Class 3 according to ISO 10648.2 Hourly leakage: 0.1 l/h Volume loss per hour: 1%
Gloves	Glove adaptable to users Different sizes available Different materials available
Power consumption (in watt) for the entire module	<3000W
User interface type	Colour 12'' Touchscreen panel display installed in a way that can be operated both from TH side and from WA side.
Electrical feed line	220-240 V -50/60Hz - 16A Monophase + ground
Compressed air	Filtered air (particles free) 6 bar
Laboratory gas lines (depending on process)	CO_2 N_2
Vacuum line for particle counter	Required Available as option
Interface	An RJ45 port available to connect the unit to the local LAN

AERAULICS SPECIFICATIONS – TRANSFER HATCH

Type of airflow	Vertical Laminar Flow on tray Turbulent Flow in waste volume
External air percentage	100%
Recirculation air percentage	0%
Type of filters on inlet air	1 H10 and 1 H14 filters in series
Type of filters on exhaust air	1 filter H14 (EN1822)
Air flow velocity on tray (with right side product inlet door closed)	0.30 m/s ± 20% Automatic controlled
Air flow velocity through the right door (with right side product inlet door opened)	> 1 m/s ± 20%
Internal differential pressure (with right side product inlet door closed)	+30Pa ± 5Pa Automatic controlled
Internal differential pressure (with right side product inlet door open)	0 Pa - Dynamic pressure equal to a minimum air velocity on side aperture higher than 1.0 m/s
Cleanliness classification (on tray)	Class A (GMP/EU)
Time to reach required class A after door closure (in a laboratory class D)	< 120 sec. Controlled by continuous particle counting that allow WA door opening only if class A is reached

AERAULICS SPECIFICATIONS – WORKING AREA

Type of airflow	Vertical Laminar Flow on working surface
External air percentage	15%
Recirculation air per centage	85%
Type of filters on inlet air	2 filters H14 (EN1822) in series
Type of filters on exhaust air	1 filter H14 (EN1822)
Air flow velocity	0.30 m/s ± 20% Automatic controlled
Internal differential pressure	+50Pa ± 5Pa Automatic controlled
Cleanliness classification	Class A (GMP/EU)

THE MANUFACTURING SITE

The experience of Bioair in manufacturing Contamination Control Equipment dates back to the early 70s', when the brand "Gelaire" became the "gold standard" for airborne contamination control in many laboratories throughout the world.

Today, in a plant located in Siziano (Pavia) and occupying more than 2,800 square meters, Bioair manufactures a complete range of Microbiological Safety Cabinets, Laminar Flow Cabinets and CO_2 Incubators produced thanks to suggestions received from the scientists and the competence of a team of skilled engineers and dedicated workers. The entire range of equipments is designed to provide the maximum level of safety, when they are used according to GLP/GMP in their respective environments.

The core business of the recently established Industrial Team is the design, manufacturing and validation of equipment for operator and product protection within pharmaceutical and healthcare production facilities, to offer dedicated and complex equipment like the ISOCell PRO Isolators.

THE R&D LABORATORY FOR REGENERATIVE MEDICINE

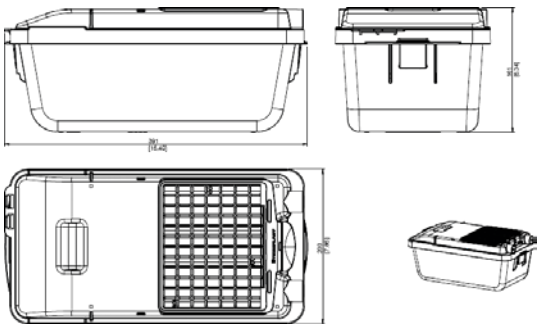
The R&D laboratory for Regenerative Medicine is focused on product development dedicated to regenerative medicine in clinical application. The laboratory for Regenerative Medicine is the core of R&D in Bioair group and it is located in the Molecular Biotechnology Centre of Turin University. The cell therapy TEAM laboratory includes scientists skilled in cell biology, stem cells manipulation and protocols development in compliance to GMP regulation.

The R&D Lab for the Regenerative Medicine transforms protocols from basic research into clinical application using stem cells manipulated in the isolator thus guaranteeing an A-grade aseptic environment to produce cells and tissues in compliance with the GMP.

ADVANCES THERAPIES TOOLS, REAGENTS & CONSUMABLES

IsoCell BIOBOX (Patent pending) is designed to contain culture flasks, tubes and other sterilized materials to mantain the consumables in a biocontainment environment.

The IsoCell BIOBOX allows the gas exchange during the growth of the cells in a incubator. You can trasfer your cell culture from one incubator to another maintaining class A environment.



PRIMO® triple packaging plasticware

The Primo®3PACK plasticware has three individual tear-to-open bags , all the tears are positioned at the TOP of the packages Inner bag is labeled with relevant product information, LOT and EXP

Media & Buffers in Single sanitized packaging

The most common potential forms of contamination in cell cultures are bacteria (including Mycoplasma), yeasts and fungi, and these can be readily assessed on a routine basis. To avoid sources of contamination in cell factory or in our ISOCell PRO Isolator, we offer a CLEAN SOLUTION TO SUPPORT YOUR CLINICAL TRANSLATION.

IsoCell GROWTH: human platelet lysate

IsoCell GROWTH is a cell culture growth supplement obtained from human platelet lysate that allows the proliferation of cells in an animal-free condition.

Collagenase from Clostridium histolyticum / SERVA*

Collagenase plays a crucial role in isolation and passing of stem cells dedicated to transplants into humans. Collagenase NB 6 GMP Grade is applicable to tissue dissociation such as isolation of human ADSCs, stem cells, chondrocytes, fibroblasts, neuronal and endothelial cells.

*Available from Bioair only for Italian market

BioAir S.p.A.
Via Figino, 20/22
20016 Pero (MI) Italy
T +39 0382 66721
M info@bioair.it

www.bioair.it