Euro Clone

ISOCell PRO

Advanced therapy isolator

Euro Clone

serving science through innovation

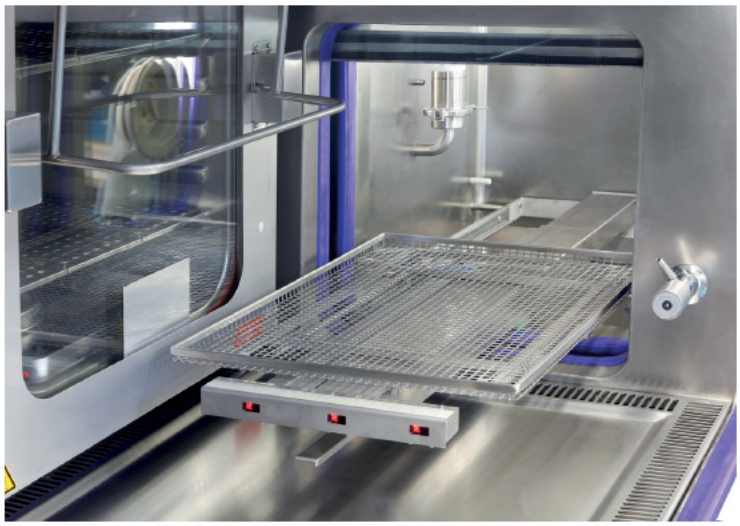
Everything you need for cell therapy products at your hand

Producing artificial tissues and cell cultures 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:

- Regenerative Medicine
- Cell/Tissue Therapy
- Gene Therapy
- Stem Cells Therapy



An **ISOCell PRO** unit installed in the
Centre de Production Cellulaire at CHUV – Lausanne (CH)

EuroClone, 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 designed to be used in validated GMP processes**

In 2014 SwissMedic started the final phase of validation for a cGMP process at the Centre de Production Cellulaire (CHUV - Lausanne) where are installed six ISOCell PRO units. By achieving this goal EuroClone'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

Traceability

Important parameters are monitored and may be recorded: the ISOCell PRO has an integrated Supervisory Control And Data Acquisition (SCADA) managing system that comply 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.

Unidirectional airflow

The main working area is kept at an ISO4.8 environment (Class A), 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 aperture of the product inlet in order to keep the internal environment clean and allow for a fast recovery of the ISO4.8 environment (Class A).

Integrated microscope

To allow fast and easy observation of the cell and tissue sample without the need to leave the clean area a microscope is included in the working 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 panel PC

Stainless steel structure

Internal and external surfaces in AISI304 stainless steel.

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 allow to disconnect the bin only if the port is closed and allow to re-connect a sterile bin without loosing the sterility both of the isolator and of the internal volume of the bin.

Integrated CO_2/O_2 incubator

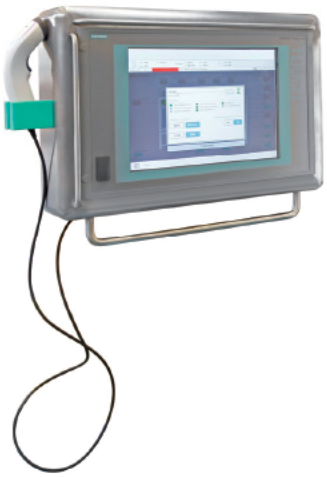
The incubator is a custom device design to fit into an isolator environment and connected to the SCADA system in order to monitor all the controlled parameters.

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

Panel PC control system

The isolator is controlled by a Siemens panel PC control system.
This assures repeatable, reliable operation.
The system is provided with networking interfaces allowing for remote monitoring and control of the isolator.

- The operator control panel is a 15" color touchscreen, which provides access to the PC for parameter setting (by authorized persons) and critical parameter monitoring. Alarms are also clearly presented on the display.
- The visual interface is designed to provide all the necessary information to the user in a quick and reliable way, allowing for optimal control and safety.
  The swinging monitor can be freely rotated in order to always provide the user with optimal visibility.
- The software has the ability to visualize user defined procedures to reduce the risks of errors. In order to improve effectiveness the procedures can be navigated using two pedals: no need to interrupt the work to turn page!
- The touchscreen has an USB port on the front and is predisposed for barcode connection for the eventual implementation of a data record for materials and products in/out



Sterilization

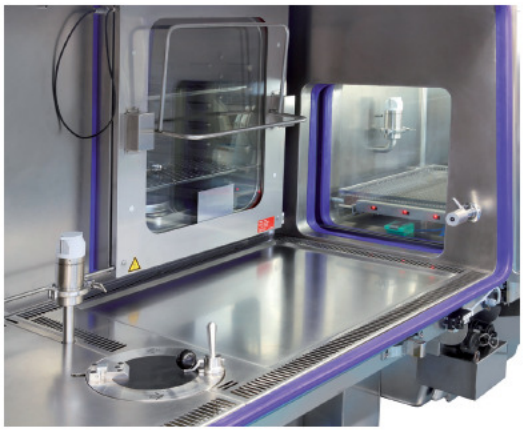
In order to guarantee a sterile environment, the ISOCell PRO is designed to allow sterilization with hydrogen peroxide vaporisation.

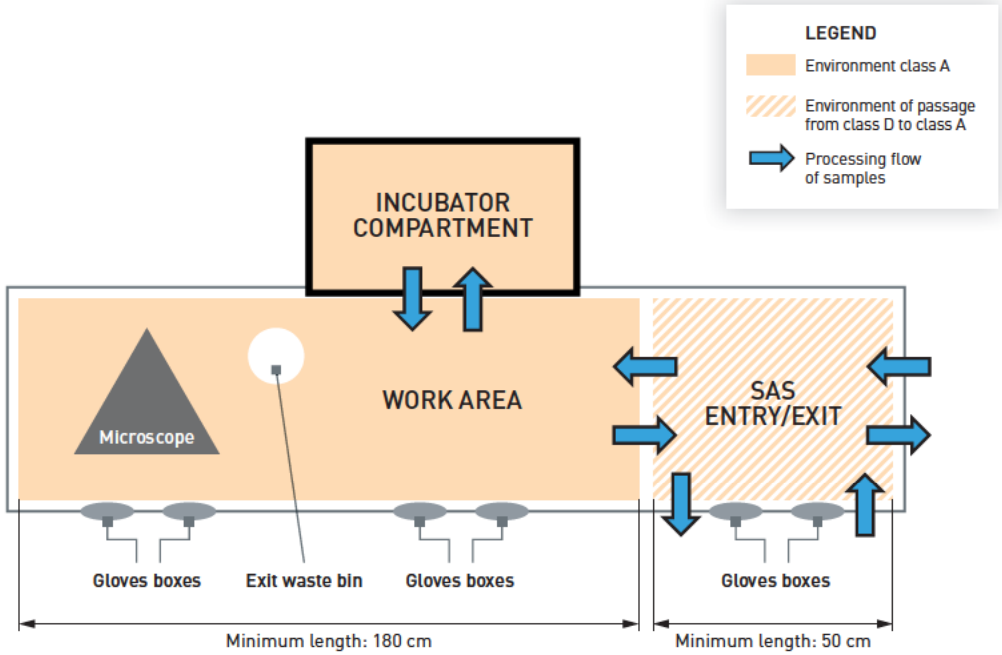
The sterilization can be done for the whole isolator (transfer hatch and working area at the same time) or for the transfer hatch only. This allows to quickly sterilize materials before introduction in the working area, reducing reagent consumption and avoiding interruption of the workflow.

- 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

The cost-saving alternative to a cleanroom

- **Closed System** – Requires only ISO 8 – Class 100,000 – Grade D surrounding environment
- **Positive Pressure Isolator** that guarantees ISO 4.8 – Grade A environment in the working area (aseptic conditions according to GMP). Positive Pressure avoids inflow contamination
- No need of a Biological Safety Cabinet Class II
- Integrated CO_2 incubator
- Easily validated at affordable costs
- Decontamination (H_2O_2) is automatic, fast, safe and economically affordable
- No need of specific *Cleanroom compliant* consumables (in particular no need of special operators' clothes)
- No need of interlocked doors, airshowers, etc.





Your project, our solutions

Euroclone and its partners are able to provide a complete support for your project and requirements.

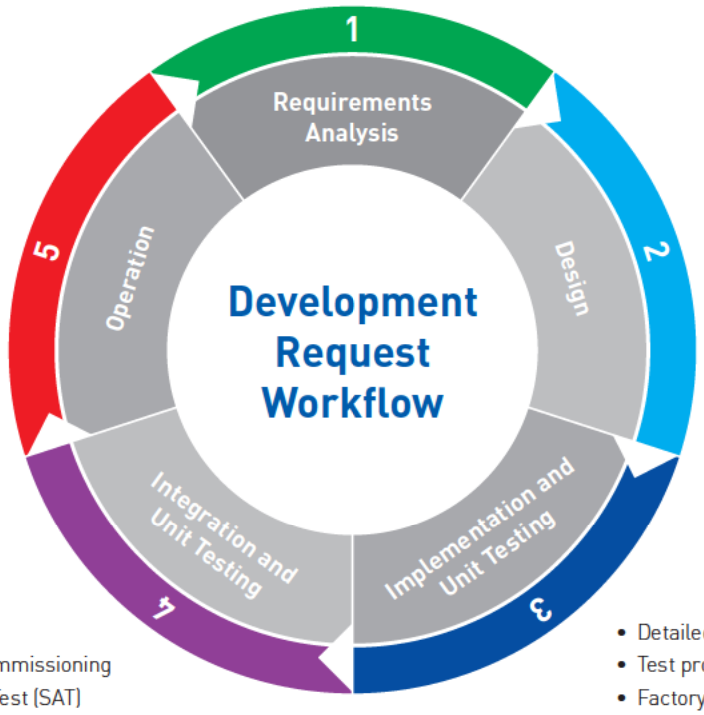
We believe that assisting the customer from the planning phase, through the realization of mock ups and identification of technical solutions to meet process requirements, installation and training, until the final steps of validation and follow-up is the key for a successful project.

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 toward a common goal!

- URS definition
- Customer Process analysis



- Mock up realization
- Isolator customization
- Definition of final layout

- IQ/OQ/PQ
- Validation process
- Full scale production

- Detailed design & construction
- Test protocols definition
- Factory Acceptance Test (FAT)

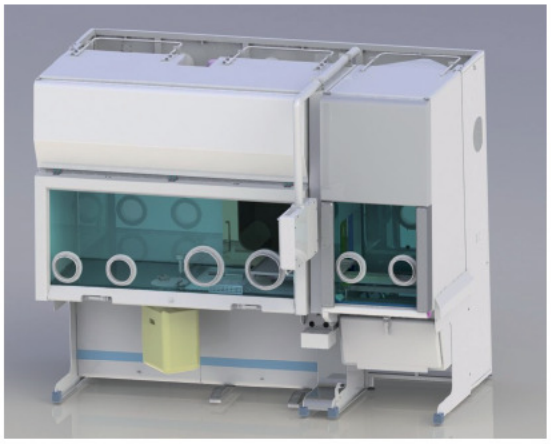
- Shipment
- Installation & Commissioning
- Site Acceptance Test (SAT)
- Training

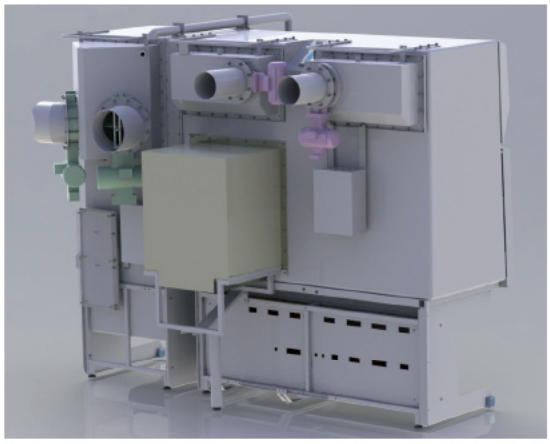
Technical Specifications

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

ISOCell PRO comply with the following European Directives and is design with reference 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)	<50 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 4.8 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	<2500W
User interface type	Colour 15" Touchscreen panel display installed in a way that can be operated both from SAS side and from WA side.
Electrical feed line	220-240 V 50Hz - 16A Monophase + ground
Compressed air	Filtered air (particles free)
	6 bar
laboratory gas lines (depending on process)	CO_2 N_2 O_2
Vacuum line for particle counter	Required Available as option

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	2 filters H14 (EN1822) 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 contolled
Air flow velocity on tray (with right side product inlet door opened)	0.45 m/s ± 20% Automatic controlled
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)	< 1 minute 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	10%
Recirculation air percentage	90%
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)

Every Lab
Every Day

EuroClone® is virtually able to **meet all needs**, in terms of *reagents, equipment and know-how*, which may arise in any of the following *markets*:

BIOTECHNOLOGY (Research and Production) *offering products for*:
Cell Biology; Molecular Biology; Proteomics; Contamination Control Equipment for Research & Industrial Application

DIAGNOSTICS (Human, Agro-Food and Veterinary) *featuring*: Cytogenetics; Food Control; Animal and Plant Infectious Diseases

MEDICAL DEVICES (both for General and Specialistic application) *to be used in*: General Surgery; Laparoscopy; Gynaecology; ENT Neurosurgery

The **Corporate Headquarters**, located in Pero (nearby Milan), coordinate the activities of 2 *satellite sites* as well as the sales efforts of more than **70 Distributors worldwide**, covering the most significant countries throughout 5 continents.

EuroClone® headquarters
Pero (MI)

Production site
Siziano (PV)

More than 40 years of experience

The experience of **EuroClone®** in manufacturing **Biohazard** and **Laminar Air Flow** cabinets goes back to the early 70s', when the brand *Gelaire®* became the *"gold standard"* for airborne contamination control in many laboratories throughout the world.

A family of **Recirculating Fume Hoods**, based on the adsorption of toxic vapors by means of charcoal filters, was successfully introduced a few years later, thus characterizing the Company as the only one really focused on the protection of the operators and inspired by its motto:

This unique know-how was cherished and brought to an even higher level of quality twenty-five years later, when under the name of **BioAir®**, the entire range was completely re-designed to meet the growing requirements of the laboratory staff and the most stringent regulations.

At the top of the range, particularly noteworthy are the **Biohazard** (or Microbiological Safety) **Cabinets**, representing the sum of the Company's know-how certified to European standards (EN12469) and complying with the Australian regulations; in other words, they are designed to provide the technicians with the maximum level of safety, when they are used according to GLP/GMP in their respective environments.

Today, in a plant occupying more than 2.800 square meters, **EuroClone®** manufactures a *complete range of microbiological safety cabinets, laminar flow cabinets and fume cupboards*, encompassing more than 15 models, with many of them available in different sizes; customized models and/or designed for specific applications can be produced thanks to the competence of a team of skilled engineers and dedicated workers.

The experience deriving from decades of sales and support to Cell Biologists, allowed **EuroClone®** to bring into the market an *extremely innovative CO_2 Incubator*, the **S@fegrow 188**, which is the result of a deep knowledge of the best conditions required by the most critical tissue culture methods, supported by the suggestions received from the scientists involved in growing cells *in vitro*.

The core business of the recently established **BioAir® Industrial** Team is the design, manufacturing and validation of customized equipment for the protection of the operator and of the product within *pharmaceutical and healthcare production facilities*.

This dedicated team will take advantage of the long experience and the production capacity acquired through laboratory LAF applications, to offer dedicated and complex equipment, ranging from **dispensing/sampling Downflow Booths** and **Clean Rooms**, to **RABS** and **Isolators** for highly active powder processing.

EuroClone S.p.A.
Via Figino, 20/22 - 20016 Pero (MI) Italy
✆ +39 02 38195.1 - 🖷 +39 02 38101465
✉ info@euroclone.it - www.euroclone.it

Quality Management Systems certified according to ISO 9001 and ISO 13485 international standards

ED1112014/isocalipro EuroClone S.p.A. reserves the right to change product specifications without prior notice