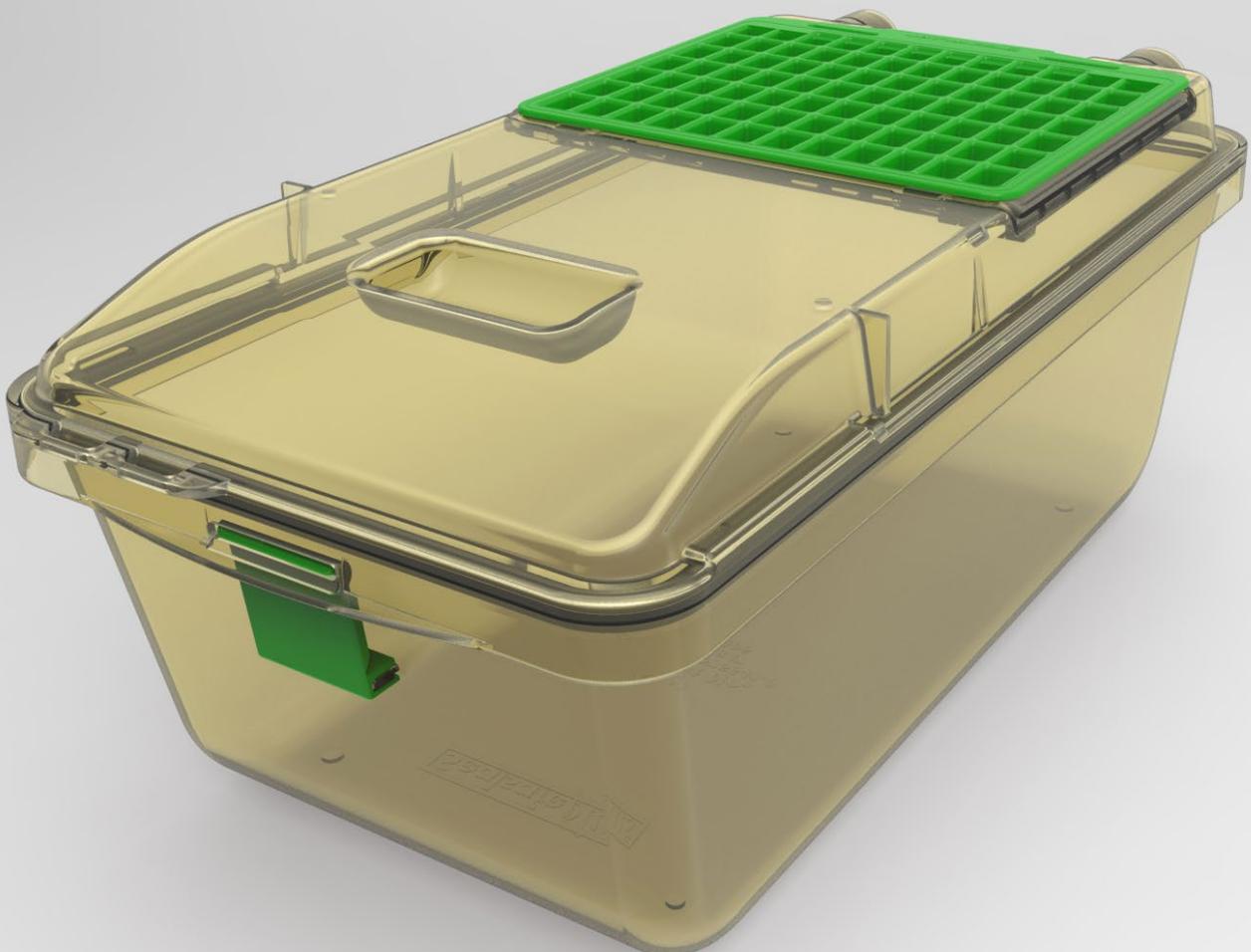




**ADVANCED THERAPY
SOLUTIONS**

IsoCell**BIOBOX**®

Closed transfer system for ATMPs productions
or applications requiring a strictly controlled
bioconfinement



The concept of bioconfinement

A new frontier in **Regenerative Medicine and in Advanced Therapy Medicinal Products (ATMPs)** is represented by the growing use of Isolators, also defined “closed systems”, instead of using classical cleanrooms (defined as “open systems”).

The use of these types of systems has become strongly recommended for the production of ATMP as established by the regulatory framework proposed by the Committee for Advanced Therapies (CAT).

The purpose of using Isolators is to set up a **bio-confined optimized working environment** aiming at **reducing production risks, management costs** and **increasing the safety of the final product**; at the same time this kind of closed system must provide a **safe working environment** also for the operators involved in the manufacturing activities.

General benefits of closed systems reduction cost compared to Clean Room

The use of closed systems such as **BIOAIR® IsoCellIPRO®** instead of the classic clean rooms open solutions, for the production of advanced therapy drugs is in fact becoming strongly recommended due to the considerable advantages obtained, both for product and operator protection and for the strongly reduced running costs incurred with closed systems compared to those relevant to open ones.

- STERILIZATION COST  **-10%**
- GOWNING MATERIALS COST  **-6%**
- VALIDATION COST  **-21%**
- ENERGY COST  **-30%**



INFRASTRUCTURAL REDUCTION

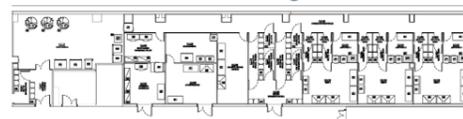
- ✓ Only Grade D surrounding environment required
- ✓ Reduction of the central air conditioning system
- ✓ No need for specific consumable
- ✓ Reduction of used surface



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 (H₂O₂ vapour)

CLEAN ROOM with 3 setting



3 ISOLATORS



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)

How to use the IsoCellBIOBOX® in aseptic mode

Introduction in the isolator of an empty, sterile IsoCellBIOBOX and sterile loading procedure. From Grade D room to work area Grade A, loading and transfer to external incubator

1. Empty IsoCellBIOBOX in the transfer hatch: closing transfer hatch external port; decontamination of the external surface of IsoCellBIOBOX;
2. Achievement of Grade A;
3. IsoCellBIOBOX lid opening;
4. Open empty IsoCellBIOBOX: communication port opening between work area and transfer hatch;
5. Automatic introduction of the tray in the work area with the open empty IsoCellBIOBOX on it (keep communication port open);
6. Loading of IsoCellBIOBOX by the work area operator (avoid touching IsoCellBIOBOX surfaces) with the flasks (or samples);
7. Automatic return to the transfer hatch of the tray with the loaded open IsoCellBIOBOX on it;
8. Closing of the communication port;
9. Loaded IsoCellBIOBOX lid closing;
10. Opening of external port of transfer hatch and transfer of the loaded IsoCellBIOBOX to external Incubator.

Introduction in the isolator of a loaded IsoCellBIOBOX coming from external incubator and sterile unloading procedure. From incubator to work area Grade A and unloading

1. Loaded IsoCellBIOBOX from external Incubator in the transfer hatch: closing transfer hatch external port; decontamination of the external surface of IsoCellBIOBOX;
2. Achievement of Grade A;
3. IsoCellBIOBOX lid opening;
4. Communication door opening between work area and transfer hatch;
5. Automatic introduction of the tray in the work area with the loaded open IsoCellBIOBOX on it (keep communication port open);
6. Recovery of the flasks from the work area operator (avoid touching IsoCellBIOBOX surfaces);
7. Automatic return of the tray in the transfer hatch with the empty and open IsoCellBIOBOX on it; close communication door between work area and transfer hatch;
8. Empty IsoCellBIOBOX lid closing;
9. Empty IsoCellBIOBOX lid closing;
10. Opening of external port of transfer hatch and removing the IsoCellBIOBOX;
11. Send IsoCellBIOBOX to sterilization.

A further considerable advantage of closed systems is that they require a **reduced space for their installation**.

At the same time, though, this implies that **less space** is available when **equipment need to be embedded into the isolator controlled work area**, or when **it is necessary to keep samples from different patients separate from each other, during the different steps of the process**.

This aspect has required the **development of new tools that should allow the biological products, such as cells or other specimens growing in flasks, to be transferred outside the isolator while maintaining the same airborne particulate classification (Grade A) as the one present in the work area of the Isolator**.

BIOAIR® has developed at this purpose a new tool, competitively priced, which facilitate the use of closed system in a GMP contest: **IsoCellBIOBOX®**

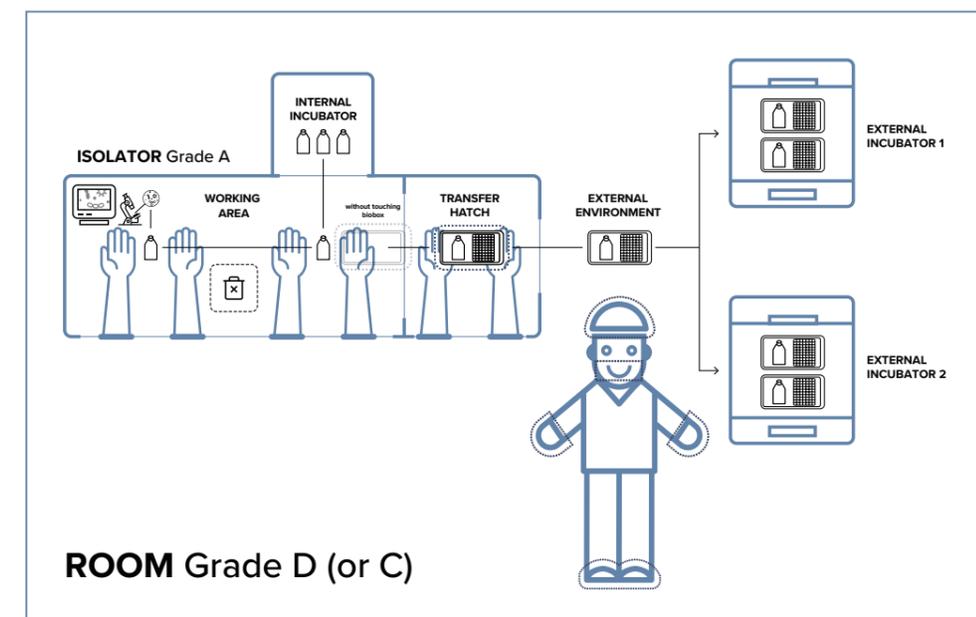


figure 1

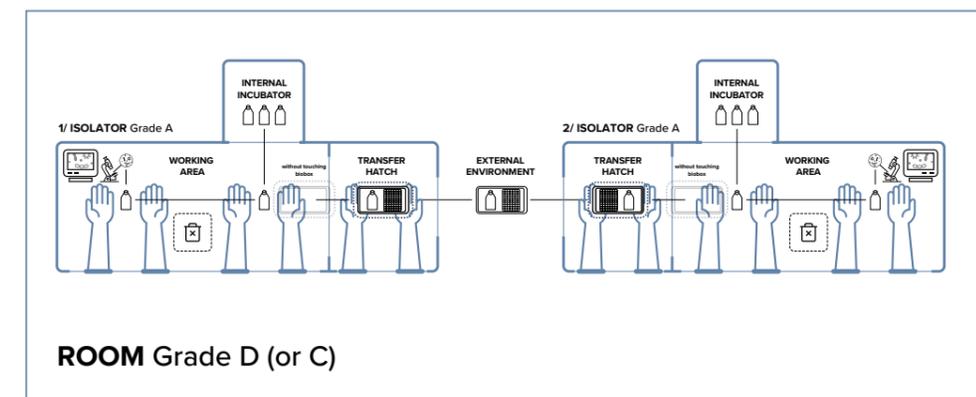


figure 2



Workflow in open system with IsoCellBIOBOX®

Obviously IsoCellBIOBOX® can easily be used in open systems as well, for transfer of samples inside the Grade B Clean Room or outside of it (figure 3).

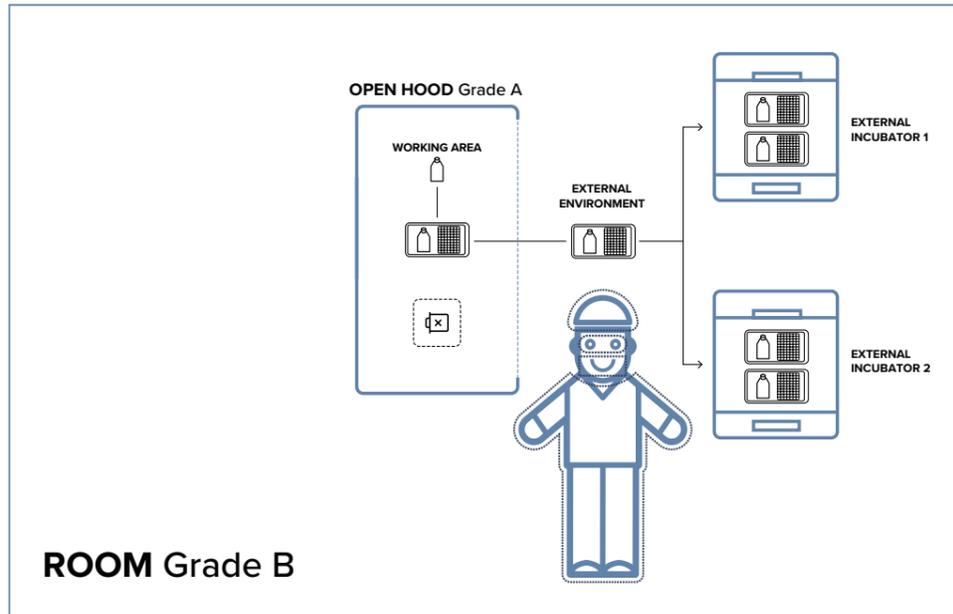


figure 3

To date, apart from some patented commercial solutions with a high economic impact, IsoCellBIOBOX® represents an **unique, reliable, GMP compliant, low-cost, easy-to-use system that guarantees the bio-confinement in Grade A** during the necessary transfers of semi- or finished products when these products are moved outside of the Grade A Isolator across the external Grade C or D environment in order to be placed into external incubators or other equipment.

IsoCellBIOBOX® provides an airtight transfer tool impenetrable to external contamination such as viruses and bacteria. At the same time, it allows to use, in closed systems solutions, standard CO₂ Incubators instead of complex and costly customized devices embedded in the isolator itself.

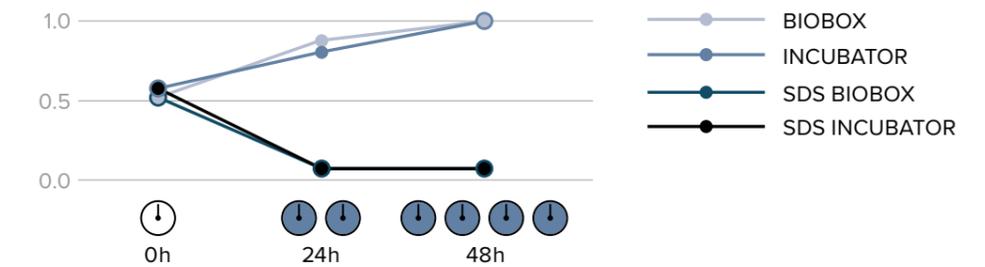
Due to its flexibility IsoCellBIOBOX® can also be used in open systems for the safe transfer of samples within or outside the controlled environment areas.

This is why it has become an **indispensable tool to be used when working in closed or open systems for ATMPs productions or other applications requiring a strictly controlled Bio-confinement.**



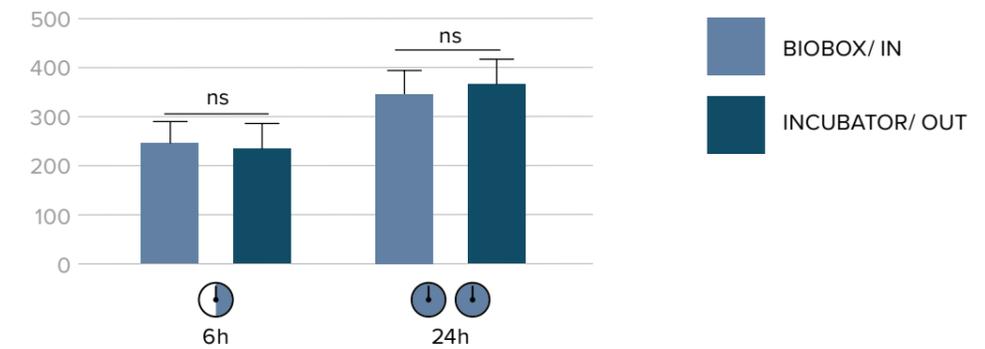
Test 1/ Proliferation

No significant change in proliferation inside or outside the biobox.



Test 2/ Wound healing

No significant change in wound healing capability inside or outside the biobox-



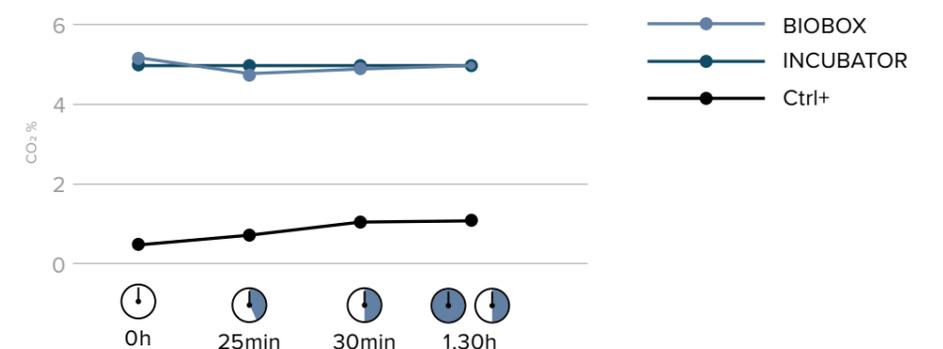
Test 3/ Western blot

No significant differences in Hsp70 protein level inside or outside the biobox



Test 4/ CO₂ levels

No significant differences in CO₂ levels inside or outside the biobox



IsoCellBIOBOX®

IsoCellBIOBOX® is a closed transfer system made in a special moulded plastic material (PSU or PPSU) resistant to thermal and/or chemicals sterilization cycles (H₂O₂) equipped with an HEPA filter membrane that allows gas exchange (CO₂ and O₂) but avoid the possibility of external particulate contamination to enter the airtight container.

AUTOCLAVABLE AND H₂O₂ RESISTANT

maximum temperature: 134°C (273°F) for 5-10 min. maximum inside and outside the IsoCellBIOBOX®



REPLACEABLE HEPA FILTER

that allows gas exchange with controlled condition for CO₂, O₂, humidity and prevent external contamination

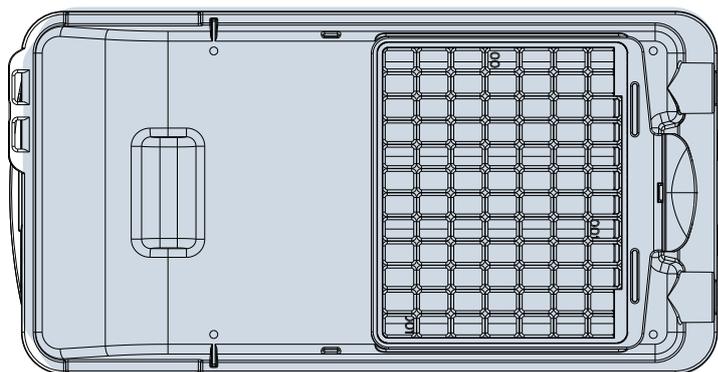
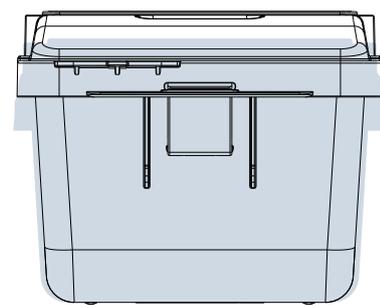
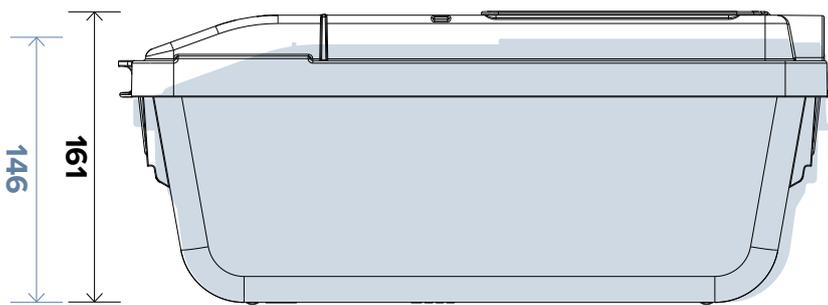


STERILIZATION AND PACKAGING

IsoCellBIOBOX® are supplied with Gamma Irradiation sterilization process and in single or triple packaging



Two Models/ sizes and capacity in number of tubes, cell culture flask, or other containers



Batch Size/ 6 IsoCell BIOBOX boxes

Ref. ESIS0106

L 391 x W 200 x H 161 mm



Flask
T25 n.25
T75 n.9



Tubes
15ml n.22
50ml n.12

Ref. ESIS0107

L 384 x W 204 x H 146 mm



Flask
T25 n.22
T75 n.7



Tubes
15ml n.18
50ml n.8



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