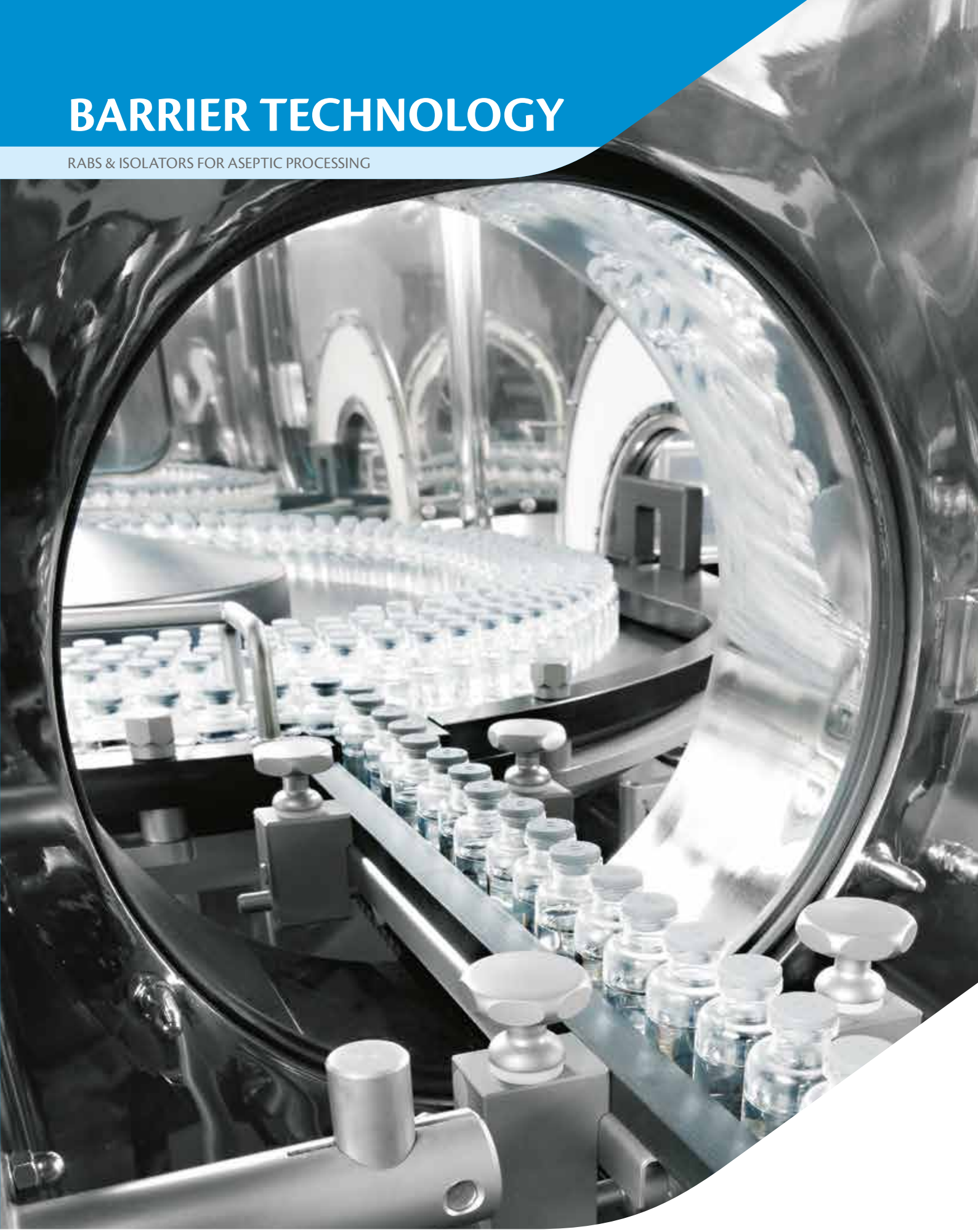
BARRIER TECHNOLOGY

RABS & ISOLATORS FOR ASEPTIC PROCESSING



IMA LIFE

Aseptic Processing & Freeze Drying Solutions

ISOLATORS

In the pharmaceutical sector the need to protect the product from contamination due to the presence of personnel or the environment is one of the major drivers for containment.
What matters most in pharmaceutical aseptic processes is the maximum reduction of the risk of product contamination which is basically due to particles and micro-organisms.

Combined with automated filling systems for liquids or powders, barrier technology minimizes the direct human intervention in the processing area and is now a technology that is being increasingly and rapidly adopted by the pharmaceutical industry.
Internationally recognized as expert in advanced aseptic processing applications, IMA LIFE has gained a wealth of experience in Cross Contamination Control and can offer a solid understanding of the risks associated with the handling of potent and cytotoxic compounds.

Barrier technology is now used with increasing frequency.

A variety of reliable containment solutions have been developed to meet customer's specific requirements.

IMA LIFE can boast an in-house technology and wide range of applications, including:

- Isolators for aseptic filling lines
- Sterility Test Isolators
- dispensing isolators
- Closed RABS
- Active / Passive Open RABS

DIFFERENT SOLUTIONS FOR DIFFERENT NEEDS

INSPIRED BY EXCELLENCE

The IMA LIFE new range of isolators combines essential features and the simplicity of proven technology with widely appreciated high standards of quality and reliability.

Example of Isolated Processing Line during Factory Acceptance Test activities at IMA plant

ISOLATORS

IMA LIFE ISOLATOR SYSTEMS CAN ENSURE OPTIMUM OPERATOR AND PRODUCT PROTECTION AND A FULL INTEGRATION ISOLATOR-MACHINE WITH COST-EFFECTIVENESS AND EASE OF USE.

The increasing amount of toxic products treated by the pharmaceutical industry calls for more and more sophisticated containment technologies that can reduce the risks posed to operators and the environment and guarantee the basic requirement of patient safety.

Consequently, the use of cleanrooms for aseptic filling and processing is going to decrease, following an inversely proportional trend related to the isolator systems demand, which are best in handle specialty environments required by some of these products as low relative humidity or low oxygen levels.
Complete vials/syringes filling lines for aseptic and/or toxic products are installed is several countries world-wide. After a difficult start, they are day by day more accepted and EMA and FDA are strongly suggesting the adoption of Isolators in any new production plant for aseptic products.

A state-of-the-art technology: a fully closed enclosure, equipped with a dedicated air circuit, where machines can be segregated. This system ensures the highest product protection and a full operator protection. Production area can be downgraded to class C and is the ideal solution to handle highly toxic products.

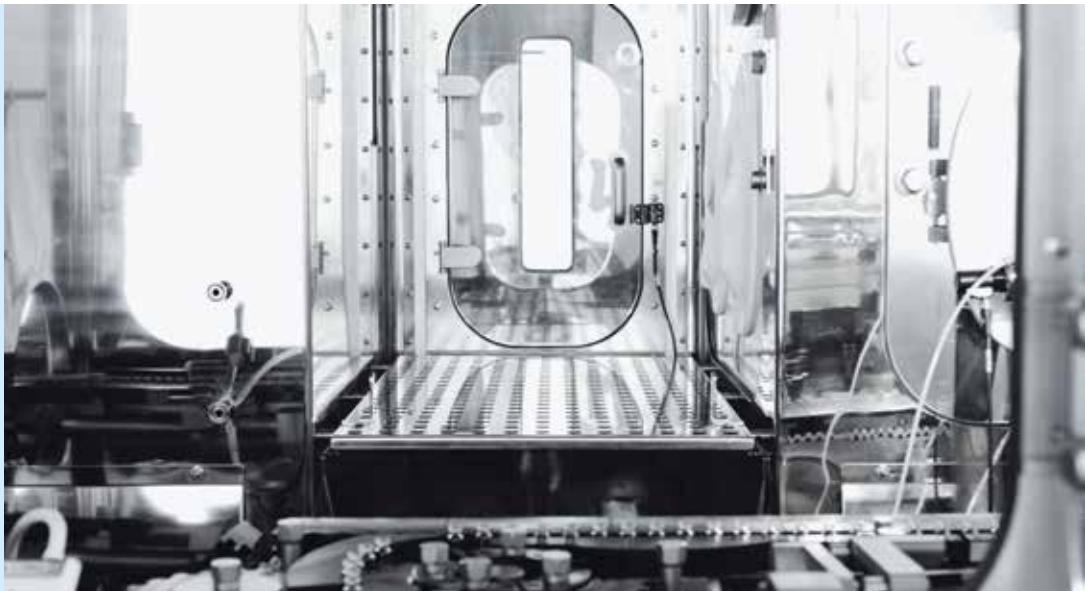
IMA LIFE ISOLATOR SYSTEMS PROVIDE THE HIGHEST AND MOST RELIABLE MACHINE CONFIGURATION TO GRANT:

- HIGHEST SAL (STERILITY ASSURANCE LEVEL)
- HIGHEST OPERATOR PROTECTION
- HIGHEST AUTOMATED OPERATIONS

MATERIAL TRANSFER ISOLATOR (MTI)

The Material Transfer Isolator is recommended to decontaminate components, tools, or whatever unit that must be introduced inside the isolated filling line, without breaking the aseptic environment.
It is a section of the "main filling line isolator" but it can be decontaminated independently, while other sections are in a different status.

Its closed environment allows fast and secure decontamination procedures using H_2O_2, ensuring a high level of aseptic environment.
It shares the same Heating Ventilation Air Conditioning (HVAC) and H_2O_2 generator system of main isolator.



Material Transfer Isolator – internal overview

OPERATION COST SAVINGS

- Less quantity of air required by the production room
- Less air sampling (particulate and microbiological)
- Less time spent by operators to enter/exit the classified room, and consequent increase of product protection
- Less expensive gowning

ISOLATION TECHNOLOGY KEY ELEMENTS

- Significant increase of SAL relative to conventional cleanrooms and open RABS
- Reduced risk of viable contamination during filling operation
- Humidity and temperature inside the isolator can be controlled adopting a dedicated HVAC
- Possibility to recycle the air used inside, saving HVAC enery consumption
- Automatic, reproducible, well documented system for bio-decontamination for all critical machine parts in situ
- Possibility to perform WIP (wash in place) cycles
- Possibility to perform automatic decontamination cycles (i.e. with H_2O_2)
- Reduced microbiological monitoring
- Reduced business risk

The following table compares the amount of conditioned air required by the same filling line, installed in the same production room, but with different barrier technologies.

	Conventional CLEAN ROOM		OPEN or CLOSED RABS		ISOLATOR	
	Filling	Surrounding	Filling	Surrounding	Filling	Surrounding
Class	A	B	A	B	A	C
Clean room area m^2	68		41	27	20.6	47.4
Air changes per hour (considering the ceiling at 3 m)				60		40
Total air per hour	110,16		66,42	4,86	33,372	5,688
Total air per day (24 hours)	2,643,840		1,594,080	116,640	800,928	136,512
Total air per day (24 hours) in m^3	2,643,840		1,710,720		937,440	
Saving respect to an installation with conventional clean room			-35.29%		-64.54%	
Saving respect to an installation with OPEN or CLOSED RABS					-45.20%	

ISOLATORS

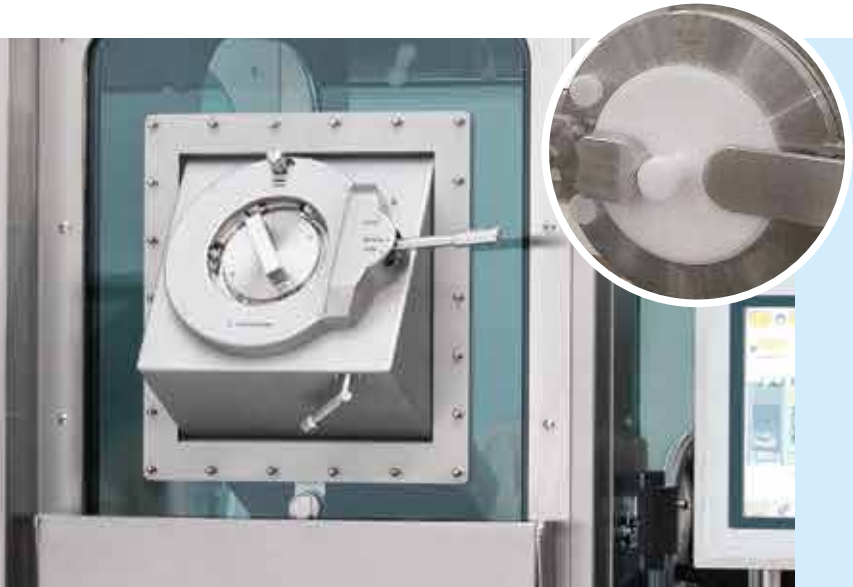
IMA LIFE SOLUTIONS ARE FULLY COMPLIANT WITH INTERNATIONAL REGULATORY STANDARDS AND GUIDELINES (I.E. FDA, EMA).

THE IMA LIFE PROPOSAL OF ISOLATORS RANGE FROM:

- Isolators for liquid aseptic production lines (aseptic and toxic)
- Isolators for powder aseptic production lines
- Isolators for lyo loading/unloading systems (aseptic and toxic)
- Sterility test isolators
- Formulation and compounding isolators
- Dispensing isolators

TYPICAL CHARACTERISTICS OF IMA LIFE ISOLATORS

- Wall Isolator - Isolator fully integrated on machine base plate – bottom of isolator is the machine base plate – no interface required
- Single Wall principle
- Sloped Equipment/Isolator base plate (to improve cleanability)
- Fully integrated design with equipment
- Easy access to the equipment operating units
- Highly ergonomic



RAPID TRANSFER PORT (RTP)

Fixed to one of the wall of the isolator, the Rapid Transfer Port system (RTP) is a bi-directional contamination-free transfer system which allows for a wide range of sterile transfer applications into and out of an isolator.

The double-lid principle of the RTP technology is usually applied for the introduction in the Class A production area of:

- Pre-washed and pre-sterilized stoppers and alu-caps
- Petri plates
- Tools, change parts, etc.

- High-grade stainless steel construction
- GMP compliant
- FDA approved material
- Automatic leak test
- HEPA filters for air inlet and exhaust
- Air handling system
- Pressure zone management
- Closed recirculation System
- Dedicated HVAC system (customized design, flexibility, modularity)
- Customized H_2O_2 cycles
- One process philosophy and one design concept for both toxic and non-toxic products
- Bag in – Bag Out HEPA filters in return ducts in case of toxic product
- WIP in air return ducts and in production section
- Spray nozzles & Spray guns for Isolator and equipment cleaning

Each section can be isolated from others by installing a dedicated cover made of PTFE, which can be easily cleaned and decontaminated.

The perfect locking is ensured by inflatable gaskets and constantly controlled by a dedicated sensor.

ISOLATORS

WALL DESIGN NO GASKETS BETWEEN ISOLATOR AND MACHINE BASEMENT ENSURING A PERFECT INTEGRATION A LONG TERM HIGHER LEAK TIGHTNESS.

H_2O_2 DECONTAMINATION CYCLES

Automatic decontamination cycles with H_2O_2 systems are currently used as rapid, low temperature techniques for decontamination of production filling lines, sterility testing isolators, sealable enclosures, and various types of pass-through systems within pharmaceutical production, research, and bio-safety laboratory facilities.

H_2O_2 decontamination cycles can be subdivided in the following steps:

- Dehumidification
- Conditioning
- Decontamination
- Aeration

IMA LIFE can supply a complete package that includes Cycle Development (CD) and Performance Qualification (PQ).

STERILITY TESTING AND DISPENSING ISOLATORS

STERILITY TEST ISOLATOR

IMA LIFE's production range also includes the ideal solution to perform Sterility Tests, drastically decreasing false positive results. Designed for QC Labs, pharmaceutical production and pharmacies, IMA LIFE's Sterility Test Isolators are equipped with an unidirectional air flow system and guarantee a constant positive pressure gradient between the chambers and the external lab environment.

MAIN FEATURES

- GMP Class A ISO 5 isolator system
- Air quality assured by Ultra Low Penetration Air (ULPA U15), unidirectional down flow and return filters
- Isolator leak tightness test according to ISO 10648-2, CLASS 2
- Integrated sterility test pump
- Fully automated bio-decontamination procedure
- Fully integrated viable and non-viable monitoring systems
- Easy-to-use integrated glove leak testing system: requires no external piping, power or compressed air

DISPENSING ISOLATOR

Designed to meet the pharma industries requirements for highest containment levels during manipulation of potentially dangerous compounds for R&D, production and QC.

MAIN FEATURES

- GMP Class C ISO 7/8 isolator system
- Air quality assured by High Efficiency Particulate Air (HEPA H14) inlet and outlet filters
- Isolator leak tightness test according to ISO 10648-2, CLASS 2
- Fully automatic or manual WIP cycles available
- Rapid Transfer Ports or High Containment Alpha/Beta valves to introduce and/or remove products from the Isolator, without breaking the containment level.
- Easy-to-use integrated glove leak testing system: no external piping, power or compressed air required

CLOSED RABS

RABS

The Restricted Access Barrier System (RABS), is a rigid protection made of transparent walls (polycarbonate or glass), equipped with an adequate number of glove flanges and gloves. It is installed on top of the filling and/or capping machines, separating them from the surrounding area.
Gloves must be positioned in order to allow the operator to perform all operations inside the machine, such as cleaning, caps/stoppers loading, vials removal, etc. so that these can be performed by operators without opening the protection walls.

CLOSED RABS

The closed RABS is an intermediate solution between isolators and open RABS. The unidirectional air flow (inlet and outlet) is fully controlled by the system, allowing a correct pressure control. The air is recycled and exhausted via a well defined channel, thus making this system suitable to be used with slightly toxic products.

Due to the lack of leak tight certification, these systems cannot be used for highly toxic products.

Class A environment must be assured whilst the surrounding must be classified as B.

Filling area

MAIN CHARACTERISTICS

- Easy to validate (air flow, air classification, doors interlocks)
- Possibility to downgrade the production area to class B
- Production area access control (doors can be interlocked)

Gaskets and details of filling area

Alu-capping area

- Automatic or semiautomatic WIP cycles
- Humidity and temperature inside the crabs can be controlled adopting a dedicated HVAC
- Possibility to recycle the air used inside, saving HVAC energy consumption
- Surrounding production area must be class B
- Limited operator protection, not useful with highly toxic products
- No possibility to perform automatic decontamination cycles (i.e. With H_2O_2)

OPEN RABS

OPEN RABS

A RABS is considered OPEN when the air used for the laminar flow is not recycled, but it is exhausted into the production room, without any control or filtration.

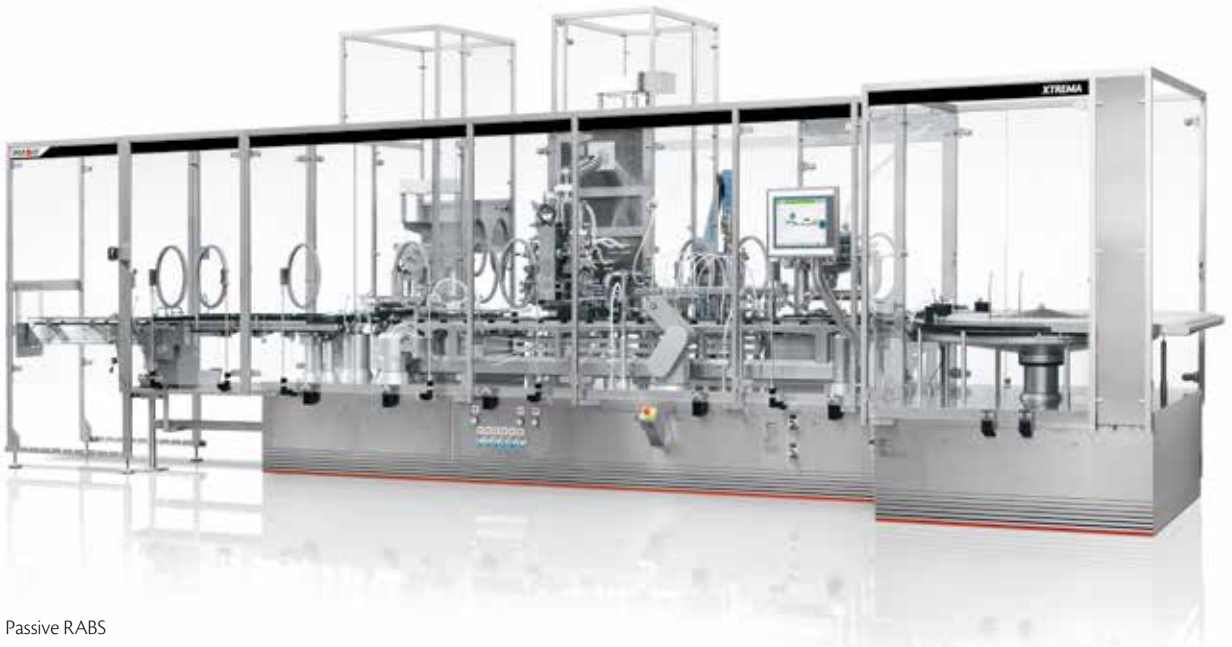
The open RABS can be either ACTIVE or PASSIVE:
- **ACTIVE**: equipped with an independent air ventilation system. In this case, the unidirectional airflow required is generated by fans and filters that are parts of the RABS itself.
In both cases, the area inside the RABS must be "A" class, and the surrounding area must be classifies as "B".
- **PASSIVE:** not equipped with a dedicated air system. In that case, the unidirectional air flow inside the RABS should be generated externally by fans and filters embedded in the false ceiling of the production room.

In both cases, the area inside the RABS must be "A" class and the sorrounding area must be classified as "B".

Active RABS

MAIN CHARACTERISTICS

- Easy to install, also on existing machines
- Easy to validate (air flow, air classification, doors' interlocks)
- Possibility to downgrade the production area to class B
- Surrounding production area must be class B (with an isolator it can be downgraded to the less expensive class C)
- No operator protection, not useful with toxic products
- Humidity and temperature inside the open RABS depend on the production room conditions
- There is no possibility to recycle the air used inside, saving HVAC energy consumption
- No possibility to perform WIP cycles (wash in place)
- No possibility to perform automatic decontamination cycles (i.e. With H_2O_2)



Passive RABS

ima.it

October 2021 - 991ZS025101

IMA S.p.A.
IMA LIFE division
Via Maestri del Lavoro 203 - 40024 Castel San Pietro Terme (Bologna) - Italy
Tel. +39 051 0296111 - Fax +39 051 0296152
marketing.life.it@ima.it