The project delivery specialists

QP Forum 2025 – Tuesday 13th May

Rewiring Pharma for the Digital age

Addressing challenges in Annex 1

Presented by Alan Kelly

Thursday 13th May 2025

Robotic Assisted Surgery

Robotic assisted surgery first took place in March 1997 on a living patient using **Intuitive Surgicals** robot known as **Mona**

Intuitive Surgicals carried out further technology advancements resulting in the FDA approval of the **da Vinci** system for general robotic surgery in 2000.

Regulatory Landscape

EUROPEAN
COMMISSION

Brussels, 22.8.2022
C(2022) 5938 final

GUIDELINES

The Rules Governing Medicinal Products in the European Union
Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use

comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with

deral Register.

-506-9136.

2 Principle

2.1 The manufacture of sterile products is subject to special requirements in order to minimize risks of microbial, particulate and endotoxin/pyrogen contamination. The following key areas should be considered:

i. Facility, equipment and process should be appropriately designed, qualified and/or validated and where applicable, subjected to ongoing verification according to the relevant sections of the Good Manufacturing Practices (GMP) guidelines. The use of appropriate technologies (e.g. Restricted Access Barriers Systems (RABS), isolators, robotic systems, rapid/alternative methods and continuous monitoring systems) should be considered to increase the protection of the product from potential extraneous sources of endotoxin/pyrogen, particulate and microbial contamination such as personnel, materials and the surrounding environment, and assist in the rapid detection of potential contaminants in the environment and the product.

development of emerging manufacturing technology may lead to improved manufacturing, and therefore improved product quality and availability throughout a product's lifecycle.

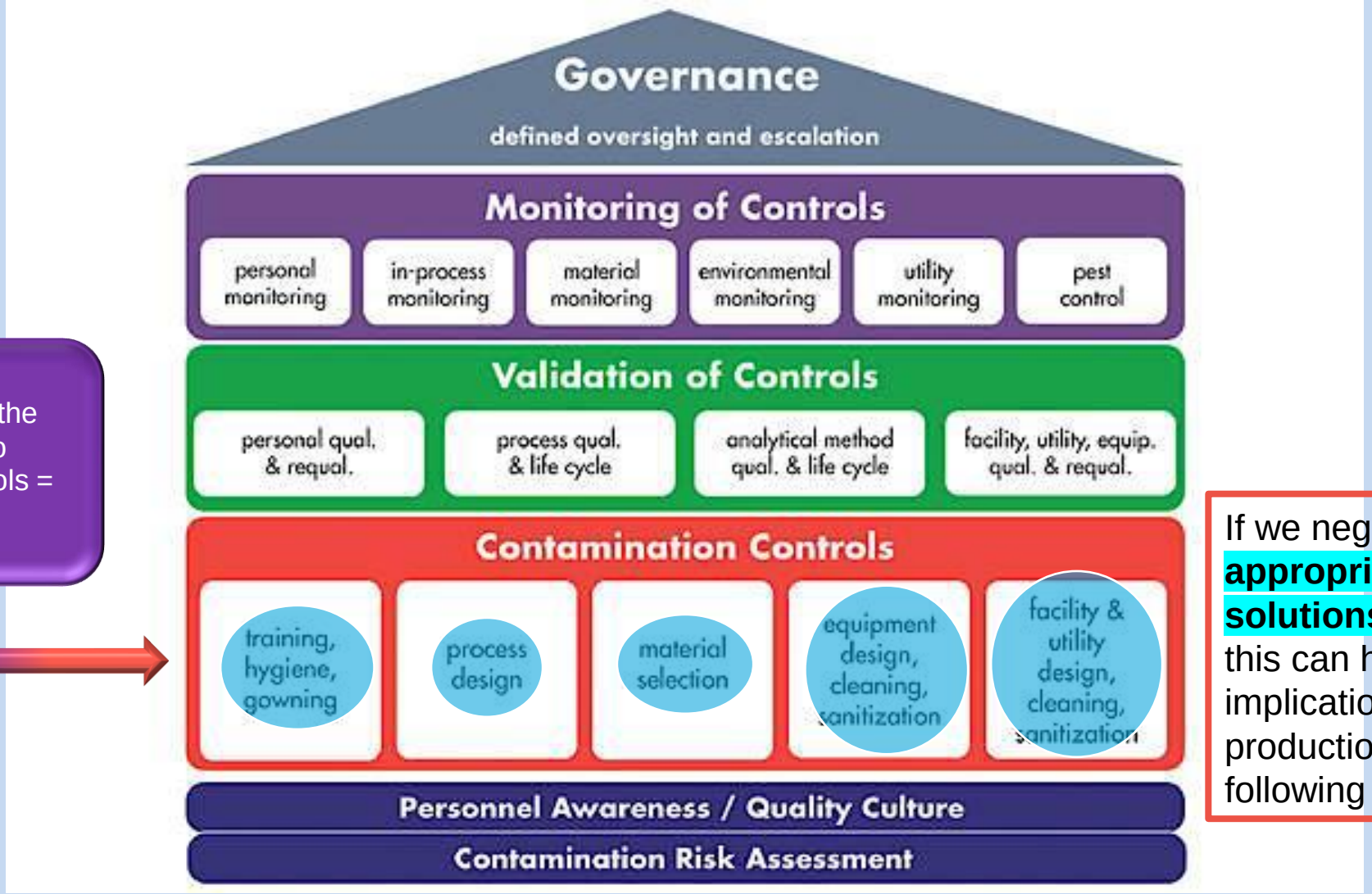
Through this guidance, FDA hopes to facilitate the application of good science and modern

8.9 Where possible, the use of equipment such as RABS, isolators or other systems, should be considered in order to reduce the need for critical interventions into grade A and to minimize the risk of contamination. Robotics and automation of processes can also be considered to eliminate direct human critical interventions (e.g. dry heat tunnel, automated lyophilizer loading, sterilisation in place).

Contamination Control Strategies must have a Holistic Focus

Contamination Control Strategy - Governance

Instead of measuring the Controls we need to Design/Build the Controls = Strategy !



If we neglect to run with **appropriate engineering solutions** at this stage – this can have major implications for production and controls following

Source: Rapid Micro Biosystems

Regulatory Direction
Annex 1

8.9

“Robotics and automation processes can also be considered to eliminate direct human interventions”

8.16

“Engineering solutions should be used where possible to minimise incursions by operators during the interventions”

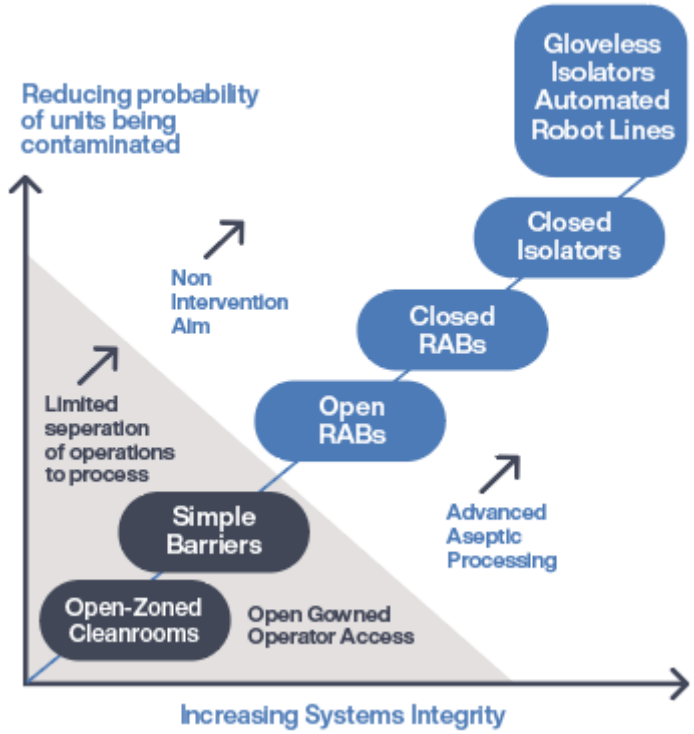
4.4

“Direct interventions (e.g. without the protection of barrier and glove port technology) should be minimised by premises, equipment….”

Progress
Aseptic Filling Industry

The Start

Filling in rooms with **Humans**



Today

Filling in gloveless isolators

New family of
Gloveless Isolator Technology

Workcell
Cytiva

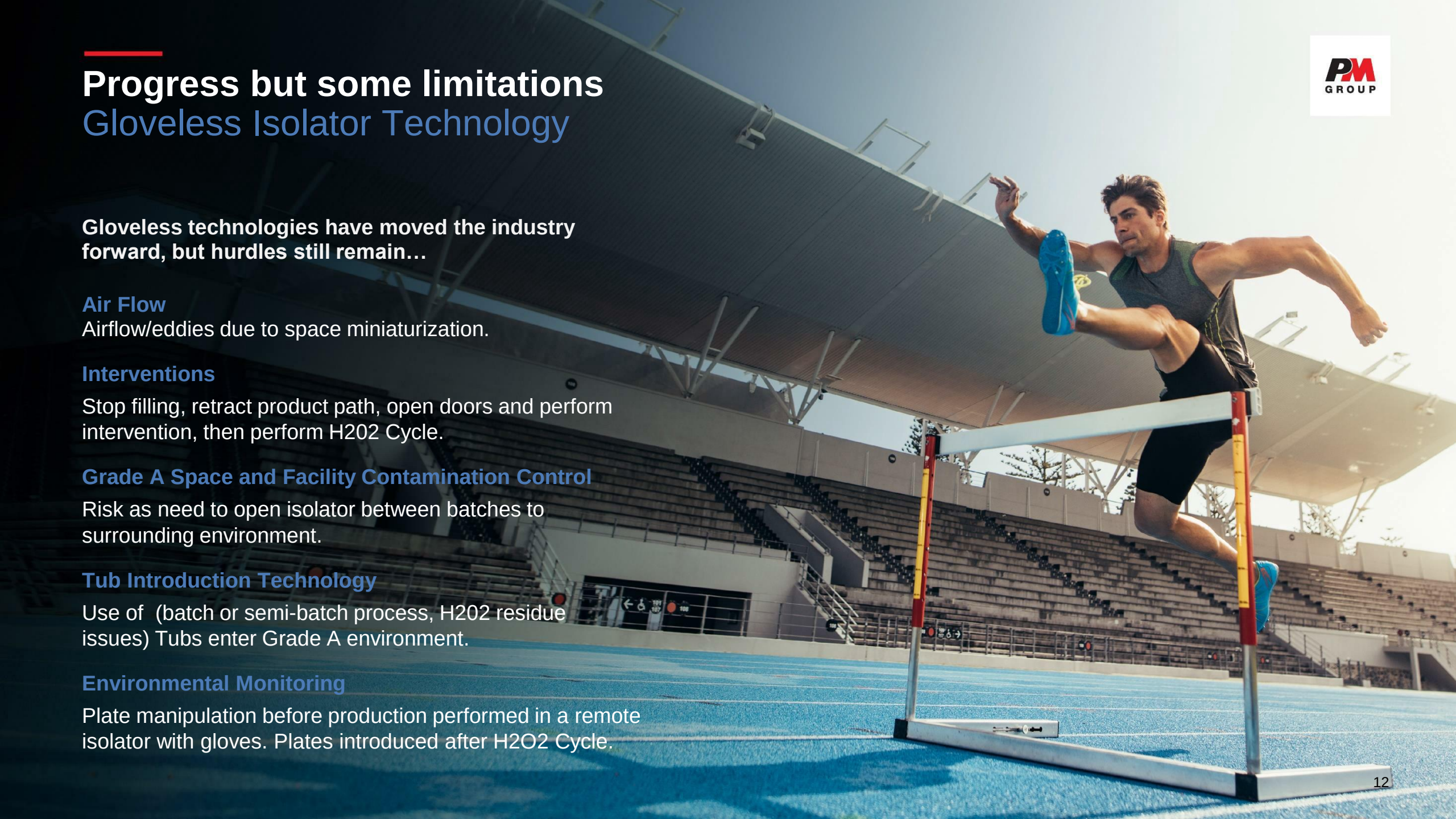
Robotic FF Cell
3P

IMA
Tile X

Robocell
Groninger

Syntegon
Microbatch

Progress but some limitations
Gloveless Isolator Technology



Gloveless technologies have moved the industry forward, but hurdles still remain…

Air Flow
Airflow/eddies due to space miniaturization.

Interventions
Stop filling, retract product path, open doors and perform intervention, then perform H202 Cycle.

Grade A Space and Facility Contamination Control
Risk as need to open isolator between batches to surrounding environment.

Tub Introduction Technology
Use of (batch or semi-batch process, H202 residue issues) Tubs enter Grade A environment.

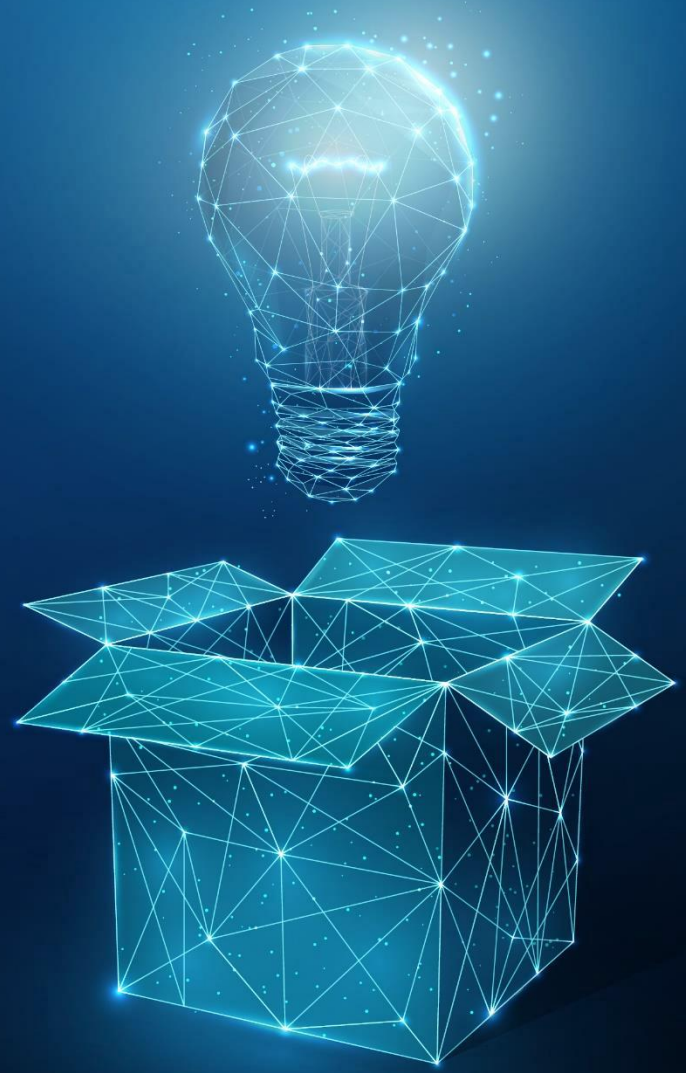
Environmental Monitoring
Plate manipulation before production performed in a remote isolator with gloves. Plates introduced after H2O2 Cycle.

Dare to achieve
through collaboration

Industry needs a different approach
to traditional legacy filling line offerings...

Thinking outside the box

with collaboration at the heart



Dare to achieve
through collaboration

Brainstorm Ideas
& Address Industry
Challenges

International
Collaborative Approach

Pharma Integration
Robotic Filling Technologies

PM Group
Process Technologies / Facility Integration

The sum is stronger
than individual parts

Azzurramicro

Azzurrasmall

Azzurrafab

Pharma
Integration

2016 > 2020

A company providing cutting-edge **robotic systems** dedicated to **small volume fill-finishing**.

Pharma Integration developed 1st commercial scale robotic filling platform with gloveless isolator.

R&D Module

GMP Isolated Filling Line in 4 Modules

2021 > Today

Further development of 1st robotic platform to create Azzurra Platform Technology, working with industrial partners PM Group and PMS.

Azzurrafab

Development of
Aseptic Filling Technology

Reducing Probability of Contamination

Open-Zoned Cleanrooms

Simple Barriers

Open RABs

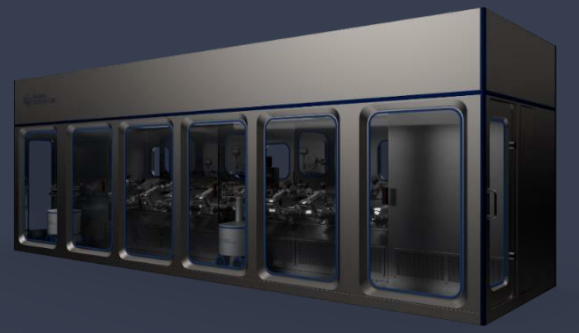
Closed RABs

Closed Isolators

Gloveless Isolators Automated Robot Line

VanRX, RoboCell, Azzurra4

Azzurramicro
Azzurrasmall



Azzurrafab

Filling in a Gloveless, Humanless, Isolated Room Enclosure with Process & Support Robots

Gloveless isolators are a recent development.

Azzurrafab

is the next step in the evolution.

Increasing System Integrity

Collaboration with Regulators
for Benefit of Industry

- Global Regulators want FASTER ADOPTION of beneficial innovative technologies.
- Workshop and review with Former MHRA Annex 1 specialist – Alan Moon.
- 2023 – Azzurra FAB invited onto FDA Emerging Technology Programme without a client sponsor…
- May 2024 – ISPE “Companies that engage with ETT were significantly more successful at advancing their respective innovations than companies that did not”
- 2 Workshops with FDA ETT:
  - Jan and Sep 2024.
  - Overall very positive engagement and reports.
  - Modifications to design and testing as a result of some comments.

Regulators

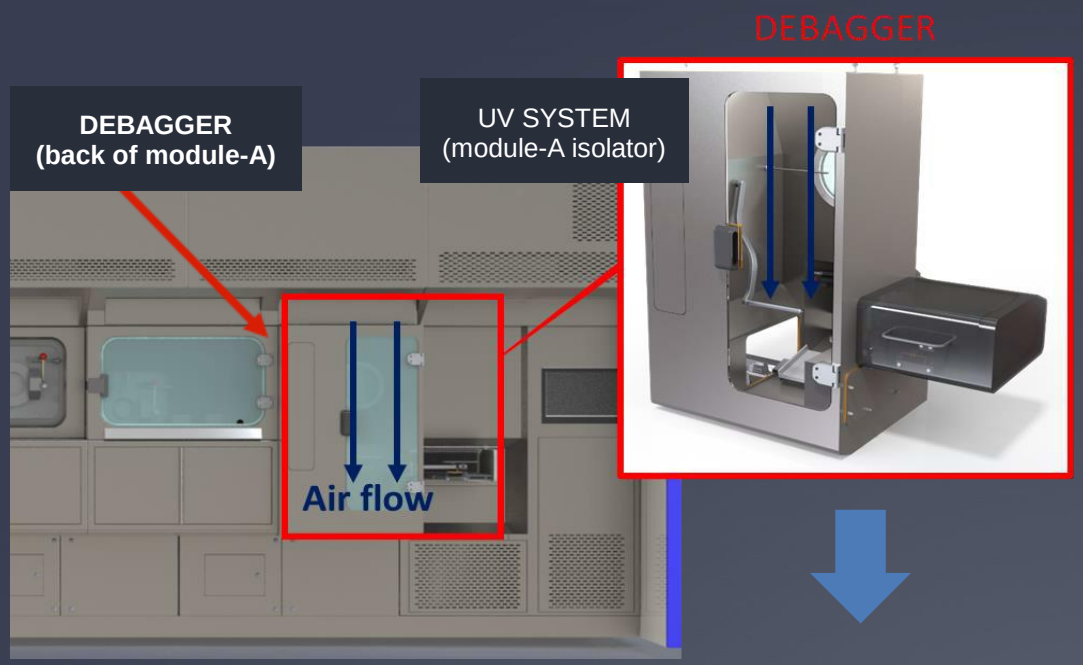
Azzurrafab

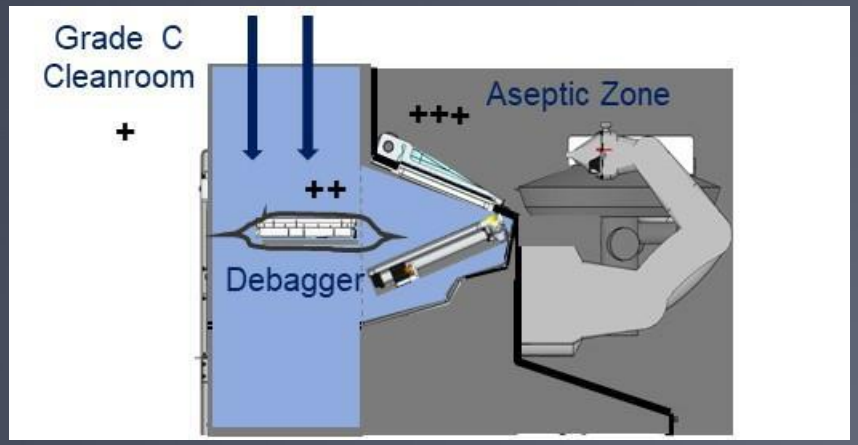
Introduction

Azzurrafab

Facility Integration

Tub Loading





- Enclosure with dedicated ventilation system **(vertical LAF**- Grade A air supply).
- **VHP decontamination** prior to production.
- **Blades** (for the cutting of the bag) are located **inside** the drawer (decontaminated).
- **Full access** (for cleaning) and **visibility** of the entire system at all stages of the process.

- Enhanced NTT with UV Decontamination.
- **No human contact** with the interior part of the bag.
- **Tub not introduced into the critical area** (inside the filling isolator).
- Transfer of bag to UV light is within 1 second with UV exposure in very close proximity.

Gloveless Environmental Monitoring

Collaboration with PMS
Two innovative patents:

Single-Use EM Plate for active viable air sampling is designed for robotic manipulation.

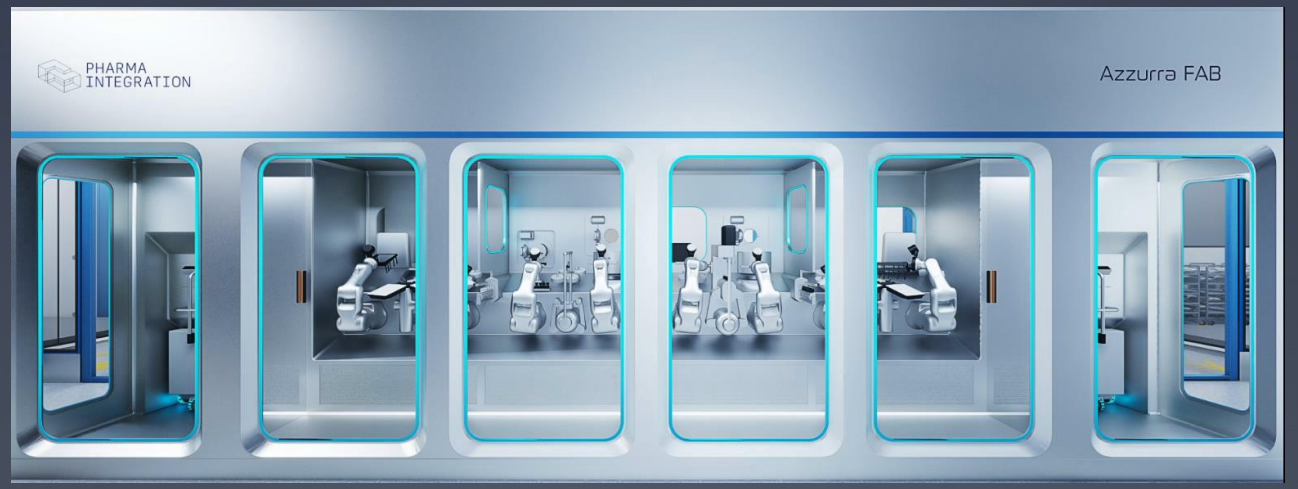
Plate is placed before H202 cycle and handled entirely by the robot.

The Robotic Rotor accommodates 4 EM plates to be positioned at the same sampling point.

Butler Robot

Dare to Believe

Next Generation Robotic Filling Platform



Fully robotized aseptic filling technology platform to support clinical and commercial.

A standardized and modular design and construction.

Overcomes many of existing industry challenges.

Part of FDA Emerging Technology Programme.

A more collaborative approach, providing a more holistic DP Facility solution.

Going back to the future

Reducing Probability of Contamination

Open-Zoned Cleanrooms

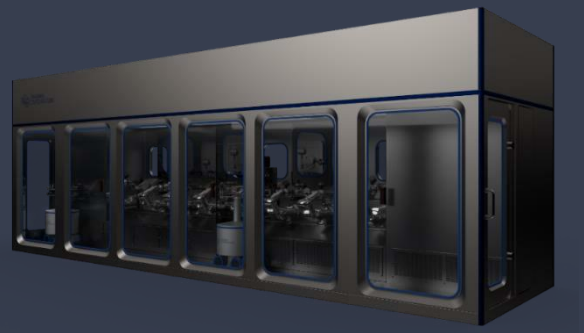
Simple Barriers

Open RABs

Closed RABs

Closed Isolators

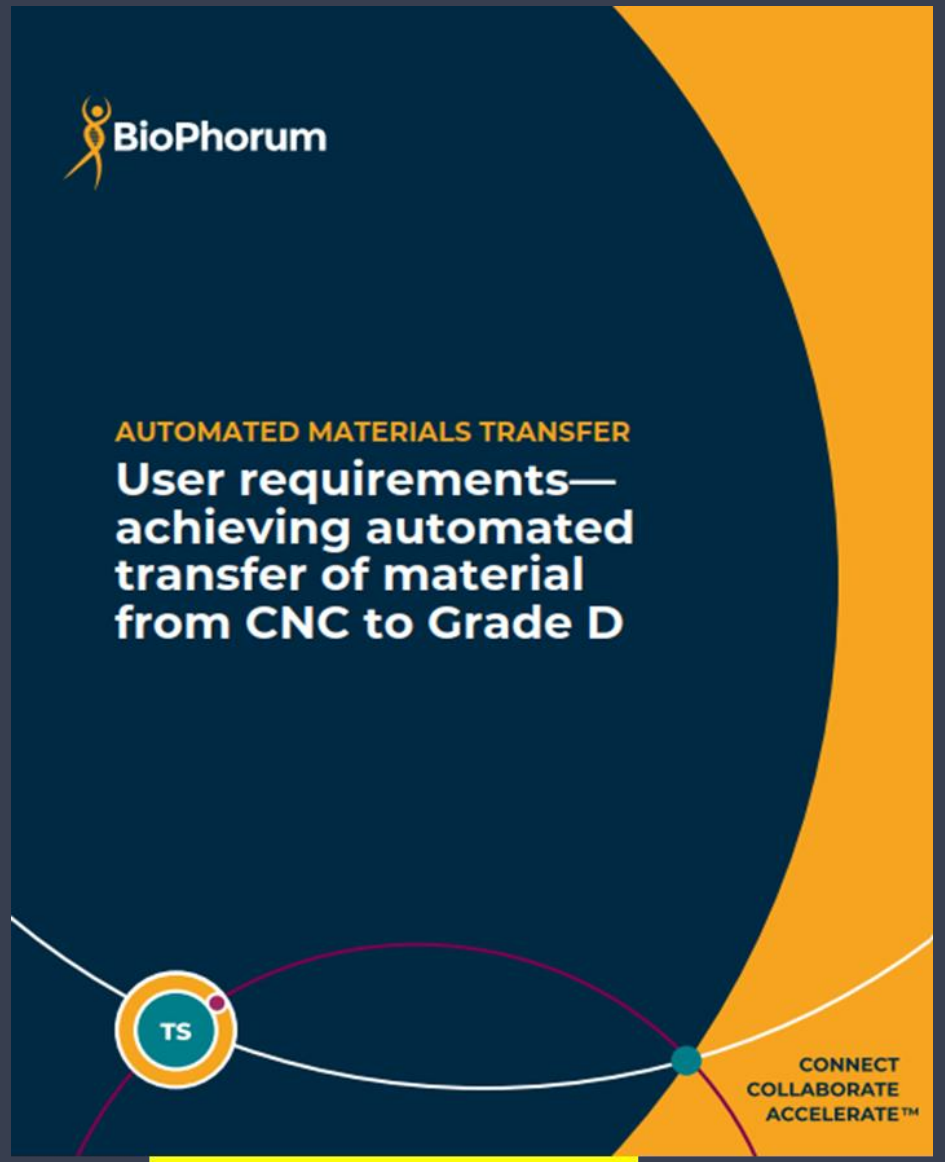
Gloveless Isolators Automated Robot Line



Filling in a Humanless Room with Robots

Filling in a Rooms with Humans

Increasing System Integrity



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Questions?

Thanks for your time today.

For more information please visit
www.pmgroup-global.com

Back-Up

Technical Details

Azzurrafab

Dimensions	8180 x 2370 x 2900 mm
Application	Vials, syringes and cartridges both RTU & bulk
Closure type	Any type – both bulk and nested
Product type	Liquid/lyo and powder
Output	3000 containers/h
Robotic system	8 Denso 6-axes robots
Decontamination Cycle	< 60 minutes
Downtime between batche	4 h

Pharma Integration operates (PI) independently from PM Group.

Azzurra Platform is marketed solely by PI.

PM Group remains independent of PI in its recommendations, whilst acknowledging our investment and close relationship with PI.

Portfolio
Technical details

	Azzurra micro	Azzurra small	Azzurra fab
Dimensions	3800 x 1800 x 2300 mm	6700 x 1800 x 2700 mm	8180 x 2370 x 2900 mm
Application	Vials, syringes & cartridges both RTU & bulk	Vials, syringes and cartridges both RTU & bulk	Vials, syringes and cartridges both RTU & bulk
Closure type	Any type – both bulk and nested	Any type – both bulk and nested	Any type – both bulk and nested
Product type	Liquid/lyo and powder	Liquid/lyo and powder	Liquid/lyo and powder
Output	500 containers/h	3000 containers/h	3000 containers/h
Robotic system	4 Denso 6-axes robots	8 Denso 6-axes robots	8 Denso 6-axes robots
Decontamination Cycle	< 30 minutes	< 60 minutes	< 60 minutes
Downtime between batches	2 h	4 h	4 h

Technical details are purely indicative and may be subject to changes without prior notice

Azzurrafab
Main Features

Modularised & Standard Design.

Room Isolator.

Butler robots interfacing with VHP Pass Box and RTP.

Monoblock allowing for pre-testing in Factory and simple Plug and Play installation leading to quicker installation and start-up times.

Able to accommodate wide variety of components – Vials/ Syringes /Cartridges / Double Chamber / Push-fit.

Designed for High potency including ability to externally wash/dry vials prior to re-nesting.

Annex 1 Compliant including Fully robotic, First Air, EM Monitoring, Aseptic Surface Monitoring (FAB), designed to support CCS.

Patented Technology

NTT & UV-C Decontamination for Tub Introduction.

EM & Plate Technology.

Butler robot.

Azzurra platform shape genuinely adhering to First Air principles.

For the AzzurraFAB

Ability to perform longer batches and campaign working using VHP P/Ts and butler robots.

Critical areas protected to surrounding environments via A/Ls.

Butler and process robots to perform interventions.

*Technology patents are either shared between PM and PI or belong to PI