MABION

Your End-to-End Biologics CDMO Partner

- Clinical & Commercial Manufacturing
- Fill & Finish
- Process Development
- Drug Characterization & Release Testing
- Preclinical & Clinical Analytics
- Regulatory & Consulting Services

Mabion's Vision

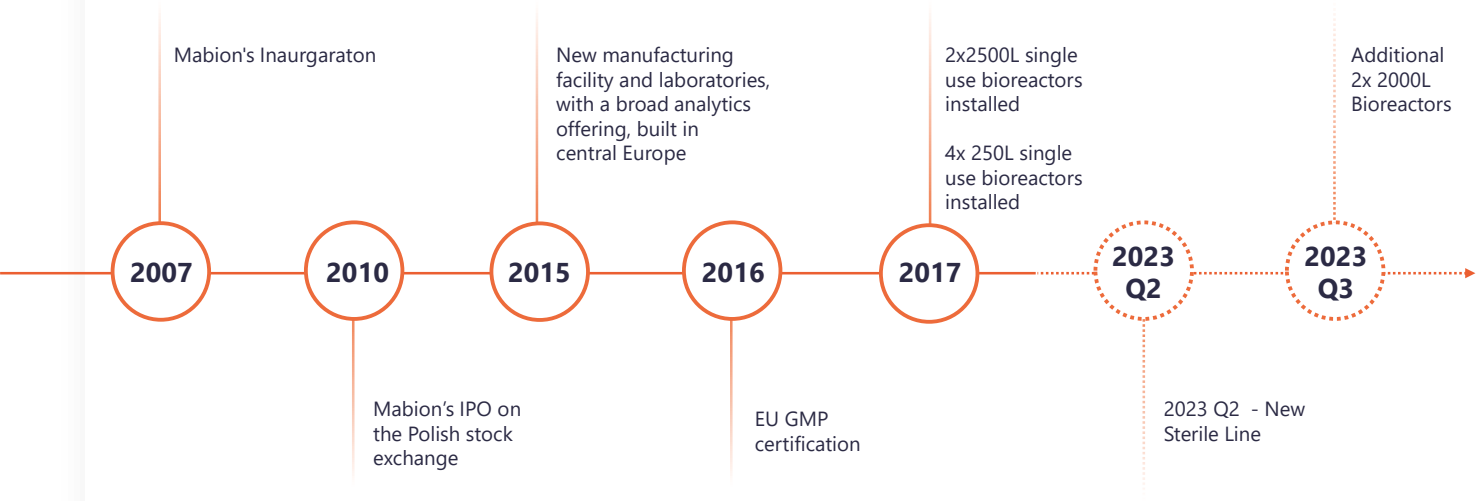
To utilise our extensive expertise in Biologic Development, Manufacturing and Aseptic Fill/Finish processing to satisfy your project requirements.

About Us

With a history that spans 17 years, Mabion has a wealth of experience in Biologic development and manufacturing, making us well-positioned to deliver on client's needs and requirements. With extensive bioanalytical capabilities and expertise in sterile manufacturing, including packaging and serialisation, we offer an end to end service.

Our Quality Management System has been inspected by various authorities including the EMA.
Trust your project with Mabion.

The Mabion History



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Locations

Konstantynów Łódzki Facility

ul. Mariana Langiewicza 60, 95-050 Konstantynów Łódzki, Poland

GMP, ISO-certified

Manufacturing (Clinical, Commercial)
Development (Process, Analytical)
Analytics (Analytical/QC services for GMP/non-GMP product testing, including Cell Based Assays)
Quality

Łódź Facility

ul. Fabryczna 17, 90-344 Łódź, Poland

GLP-certified

Bioanalytical studies (PK, PD, Immunogenicity; BSL-II labs)
Clinical project management and supporting operations

Warsaw

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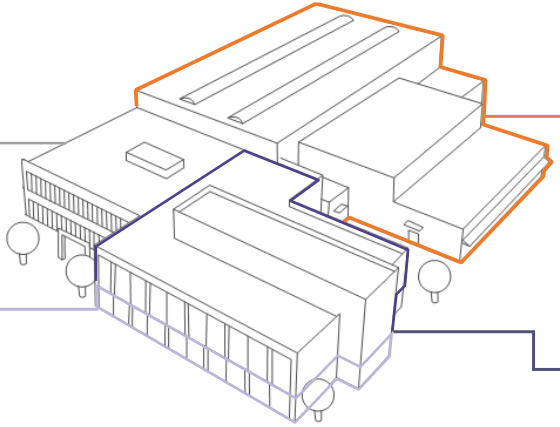
Facility Layout



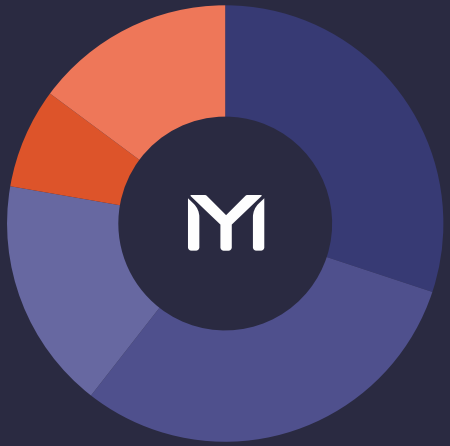
Office spaces

Manufacturing
Actual area: 2098 m^2

Quality control
Actual area: 621 m^2

Process Development
Actual area: 566 m^2

Mabion Personnel Chart



77	Manufacturing
78	Quality
44	Supporting Departments
19	Maintenence
38	Development

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Project Management

Project Management

With every project entrusted to Mabion, comes a dedicated project manager. The allocated Project Manager ensures that your project is given the utmost attention.

Our approach to Project Management is the key component for delivering the Mabion promise in providing a world-class, customer-oriented outsourcing experience by delivering on Mabion's commitments to supply, quality, service and price.

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Process Development

R&D Product and Process Development Laboratory Capabilities

- Upstream Process Development
- Downstream Process Development
- Process Scale Up
- Process Space & Process Characteristics
- Technology Transfers
- Analytical Methods Development & Validation
  - Structural Assays
  - Physicochemical Assays
  - Biological/Functional Assays
- Qtpp Establishment
- Comparability & Similarity Assessment
- Reference Standard Establishment
- Stability Studies (Ds, Dp, Freeze-thaw Studies)

Pilot processes: R&D capabilities

Process development

Process optimization from mL to thousands L scale

UPSTREAM PROCESS

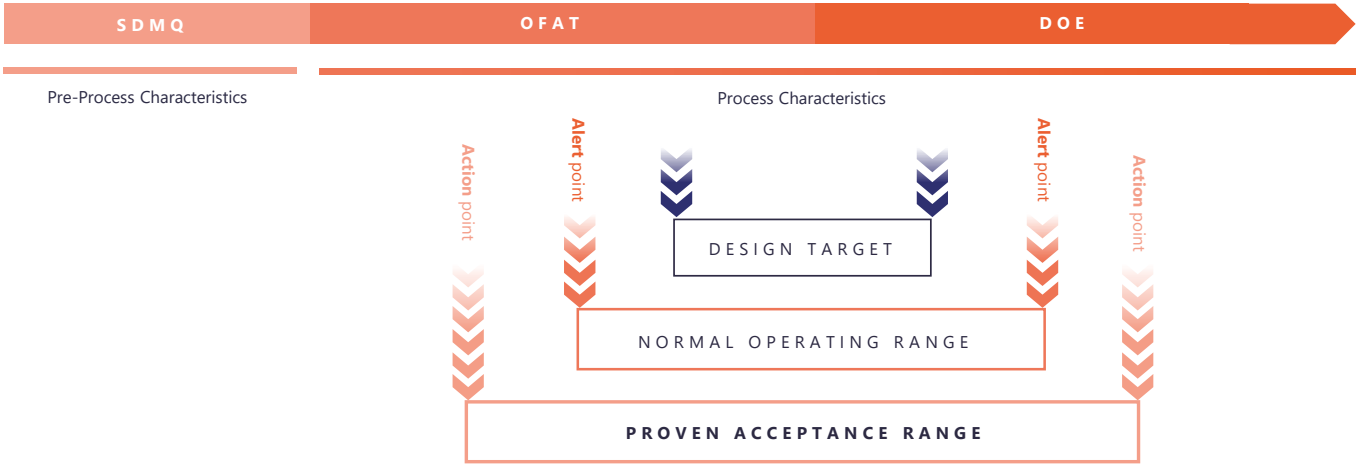
- Vector and expression system development
- Stable cell line establishment and characterization
- Cell culture optimization
- RCB, MCB and WCB preparation
- LIVCA (Limit of In Vitro Cell Age) studies
- Monoclonality confirmation studies

DOWNSTREAM PROCESS

- Chromatography based purification (eg. affinity, ion exchange)
- Filtration processes (eg. ultrafiltration, nanofiltration)
- Formulation development
- Resin lifetime studies

Process Characterisation (PC)

Mabion's approach to PC



Panel of analytical methods

Product characterisation

Functional Assays

- Cell-based assays
  - CDC, ADCC, Apoptosis, ADCP
- Protein-protein interaction evaluation
- Virus analyses

Physicochemical Assays

- Protein concentration
- Identity confirmation
- Molecular weight
- Post-translation modifications
- Glycation
- Process-related impurities
- Product-related impurities

Ultimate 3000 Q. Exactive Plus MS

Biacore T200

Vanquish UHPLC System

BD FACSVerse

Clinical and pre-clinical analytics development

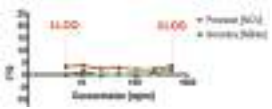
Analyzing PK, PD and Immunogenicity in clinical studies of monoclonal antibodies

Mabion R&D Center with specialized GLP-certified laboratories capable of running full-scale **PHARMACOKINETIC**, **PHARMACODYNAMIC** and **IMMUNOGENICITY** analytical panels for the purpose of Phase I-III clinical trials of biological therapeutics

PHARMACOKINETICS

Gyrolab xPlore Platform

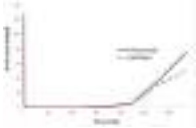
- Nanoliter-scale immunoassay generating high quality data
- High repeatability: ISR >95 % of reanalyzed samples
- High precision: for >95% reported results CV <10%
- High sensitivity (≤1µg/mL), selectivity, specificity and accuracy, with no „carry over" effect
- High throughput



PHARMACODYNAMICS

Flow cytometry on 8-color BD FACSLyric™ platform

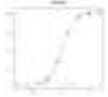
- Intra and inter-assay precision <15% of CV
- Accuracy (comparison with reference laboratory) ± 15% Bias
- Sensitivity down to 10 B cells/µL
- Whole blood sample stablity extended to 14 days at 2-8°C and to 3 days at RT
- Thermal cycle stability confirmed for 3 cycles



IMMUNOGENICITY

Immunobridging assay with acid dissociation on Gyrolab Platform and potency assay for NAbs evaluation

- Innovative high throughput Gyrolab platform
- High sensitivity (< 100ng/mL)
- High precision (CV < 15%)
- Characterization of neutralizing antibodies and titre with a highly sensitive ADCC cell–based reporter assay
- More reflective of the actual biological activity of neutralizing NAbs



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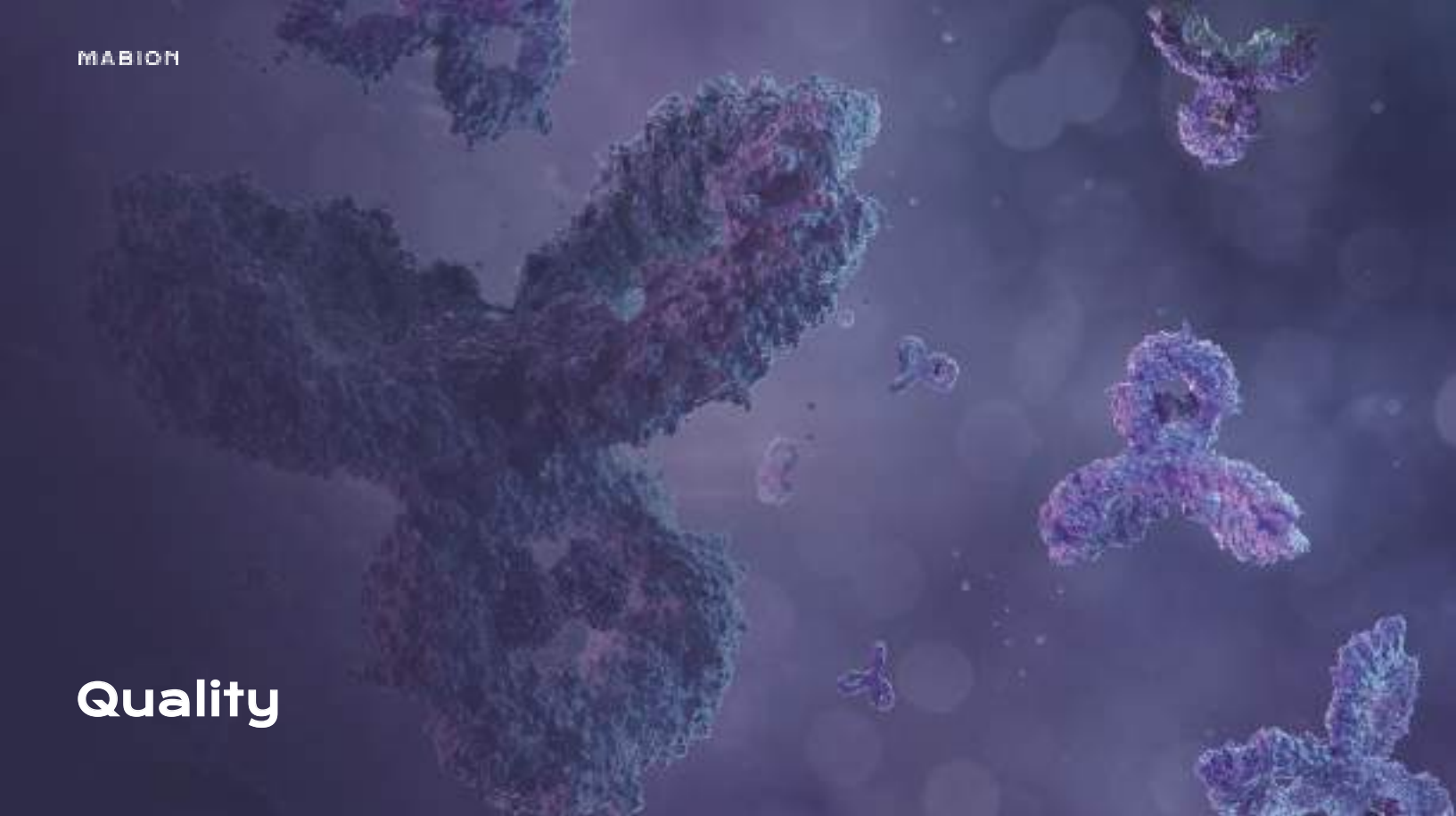

Quality

Mabion's Quality Control capabilities

GMP compliant

- QC testing of raw materials
- QC testing for in-process controls drug substance, drug product, reference product
- Analytical methods optimization, validation and transfer
- Characterization and qualification of reference standard and critical reagents
- Long term, accelerated and stress stability studies
- Environmental monitoring
- Supporting documentation

Quality Control Microbiological Laboratory

Microbial testing is performed in microbiological laboratory designed in the cleanroom technology analogous to manufacturing department (separate rooms dedicated to individual tests). Testing includes:

- Control of drug substance / drug product / cell culture : Sterility and bioburden testing by membrane filtration and direct inoculation (in accordance with Ph. Eur.)
- Microbial environmental monitoring tests for manufacturing operations and analytical operations: settle plates, contact plates, volumetric air samples, swabbing
- Pharmaceutical water and technical gas testing
- Diagnostic tests: Microscopic and biochemical tests
- Disinfective agents effectiveness testing

Regulatory supervision and consultation

Providing multi-level scientific and regulatory support to ensure the highest research standards

LEADING THE MARKETING AUTHORIZATION PROCESS

- Contact with EMA PM and solution of dossier validation queries
- Management and preparation of responses to Agency's questions (Day 120, Day 180, Oral Explanation)
- QC and submission of regulatory documentation throughtout the marketing authorization process

PARTICIPATING IN VACCINE MANUFACTURING PROCESS DEVELOPMENT, MANUFACTURE AND QUALITY CONTROL METHOD TRANSFER

Planning, guiding and overseeing the drug development process through all pre-clinical and clinical stages

Minimizing residual uncertainties by bridging the CMC and clinical data

Ensuring that the drug development process is in full compliance with the EU and US regulatory requirements

Assuring best quality and completeness of the submitted dossiers

Market analysis, searching for innovation; Creating the development strategy	Product & process Development; Structural and functional characterisation	Development of Manufacturing Quality Control & Quality Assurance	Preclinical studies PK/PD/Toxicology	Early clinical studies Phase I / II	Pivotal clinical studies Phase III	Regulatory filing / approval	Sales and marketing

Quality systems operating at Mabion include EU-GMP for manufacturing (since 2012), GLP for Bioanalytical studies (since 2014) and ISO. Mabion QMS was built following Eudralex vol. 4 principles.

As a result, robust GMP processes have been built, ready to accommodate any Client quality requirements, including compliance with US FDA cGMP

Mabion's QMS

Mabion audits and inspections history

9
GMP Inspections by GIF

7
GLP Inspections

2
ISO 9001 Inspections

9
Audits & inspections performed by external companies

5
Due Diligence audits

1
GMP Data integrity Audit

2
GMP certification

1
GCP Inspection by EMA

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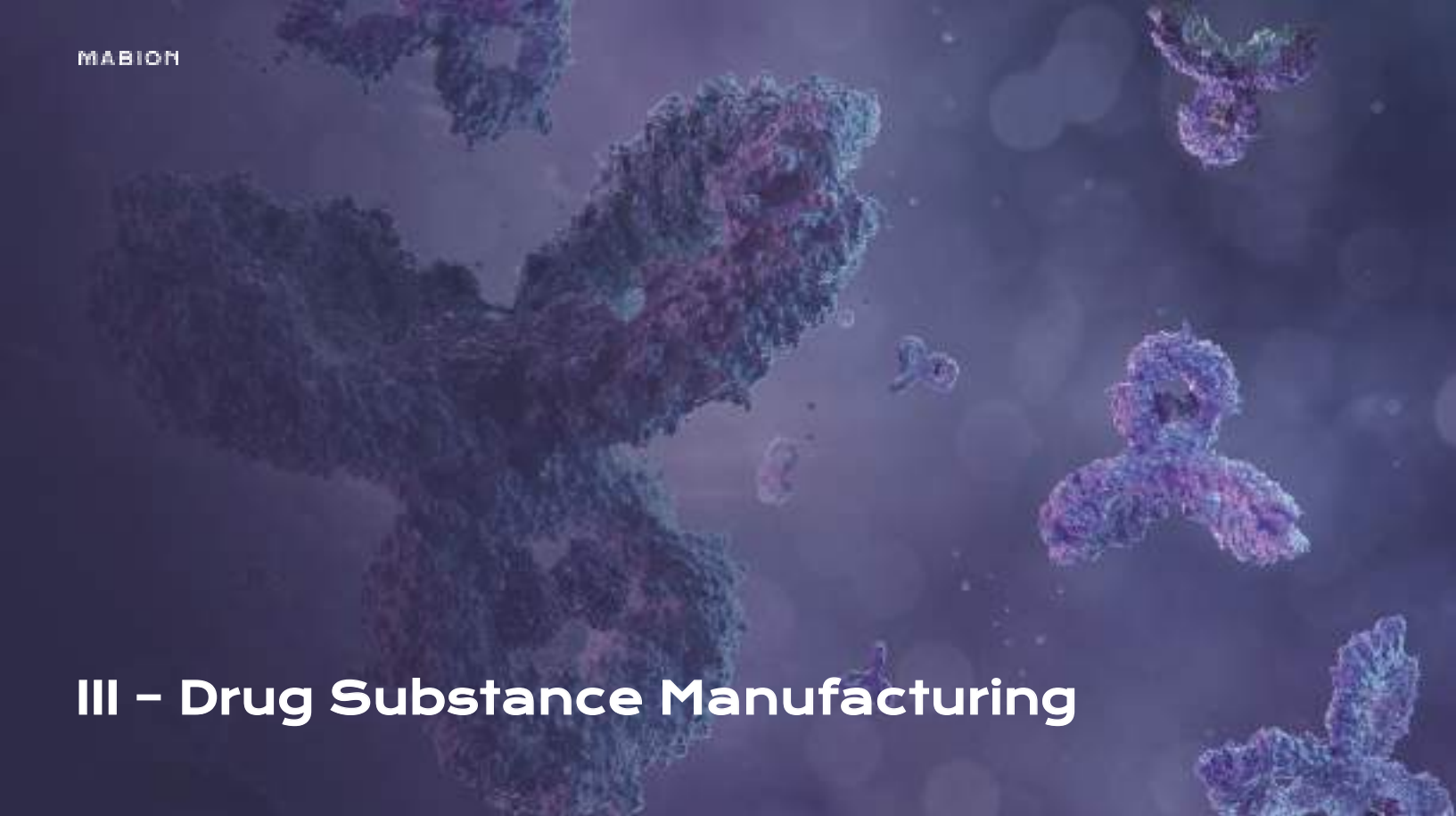

III – Drug Substance Manufacturing

Mabion's Manufacturing Facility

Good Manufacturing Practice (GMP) certified and fully integrated manufacturing facility focusing on recombinant protein technology located in the vicinity of the city of Łódź, 1hr from Warsaw.

4 × 250L bioreactors → scale up → **2 × 2500L bioreactors**

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Upstream manufacturing

USP

- **Mammalian & insect cell cultures**
- **4 x 250L orbital shaking bioreactors**
- **2 x 2500L orbital shaking bioreactors**
- **Medium & supplements preparation and storage capacity**
- **GMP MCB & WCB cell banks generation and storage**

Scope	Technologies/Description	Room / equipment
USP	Eukaryotic cell cultures - Up to 10 x 2L flasks	**B+A class room** Laminar chambers CO_2 orbital-shaking incubators, Centrifuges Microscopes
	Bioreactor cell culture - Up to 5000L	**D class room** FLEX 2 BioProfile cell analyzer and counter 4 x 250L orbital-shaking bioreactors 2 x 2500L orbital-shaking bioreactors Space for additional 2 x 2500L bioreactors
	Cell harvest	**D class room** Depth filtration FlexAct system with pressure sensors, magnetic mixer, peristaltic pump and scale Product collection, weight and transportation system Disc stack centrifuge
	Medium preparation	**D class room** Stainless steel mixtank 3000L Medium collection, weight and transportation system
	WCB preparation and storage MCB preparation and storage	Preparation of cells bank in GMP environment Storage of MCB and WCB at ultra-low temperatures (below 150°C) in the gas phase of liquid nitrogen
	Intermediate product storage	**NC** Cold rooms (2-8°C)

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Downstream manufacturing

DSP

- **Separation technologies (depth filtration & centrifugation)**
- **Affinity chromatographies, ion-exchange chromatopgraphies (CEX, Lentil Lectin, TMAE)**
- **Ultra/diafiltration**
- **Tangential Flow Filtration**
- **Nanofiltration**
- **Sterille filtration**
- **Formulation**
- **Buffer preparation**

Scope	Technologies/Description	Room / equipment
DSP	• Protein A affinity chromatography - 25L chromatography column • Lentil Lectin affinity chromatography - 26L chromatography column	**D class room** • AKTA Ready system • Product collection, weight and transportation system
	• Low pH virus inactivation	**D class room** • FlexAct system with pH and temperature sensors, magnetic mixer, peristaltic pump and scale • Product collection, weight and transportation system
	• Cation-Exchange Chromatography - 63L chromatography column • TMAE chromatography -150L chromatography column	**D class room** • AKTA Process system • Product collection, weight and transportation system
	• Anion-Exchange Chromatography in flow-through mode with single-use columns	**D class room** • FlexAct system with pH and temperature sensors, magnetic mixer, peristaltic pump and scale • Product collection, weight and transportation system
	• Nanofitration	**D class room** • FlexAct system with pH and temperature sensors, magnetic mixer and membrane pump • Product collection, weight and transportation system
	• Ultrafiltration, diafiltration • Single use membrane pomp and UF cassettes	**D class room** • FlexAct system with flow, pressure and temperature sensors, magnetic mixer, peristaltic pump, and scale (for large volume process, product pool >100 L) • TFF unit (for small volume process, product pool 10-30 L) • Product collection, weight and transportation system
	• Formulation buffer preparation	**C class room** • FlexAct system with pH and temperature sensor, magnetic mixer, peristaltic pumps, and scale
	• Buffer preparation	**D class room** • Stainless steel mixtank 3000L • Single use magnetic mixers 200L, 400L, 1000L • Buffer collection, weight and transportation system
	• Storage of DS	• NC Cold room (2-8°C) • Freezers (≤ -60°C)

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II – Drug Product Manufacturing

Drug Product Manufacturing

FILL&FINISH

- **Automated filling line**
- **Secondary packaging and serialization**
- **Product storage and transportation**

Scope	Technologies/Description	Room / equipment
Fill&Finish	• Vials sterilization • Formats: 10 ml vials, 50 ml vials	**D – A class (local) room** • Washing machine • Depyrogenation tunnel
	• Sterile filling, capping and stoppering • Disposable system for dosing needles and product-contact parts including feeding	**Local A class – open RABs** • Automatic, robotic filler
	• Product inspection	**D class room** • Optical chambers for manual visual inspection • Vacuum based leak testers
	• Storage of DP	**NC** • Cold room (2-8°C)

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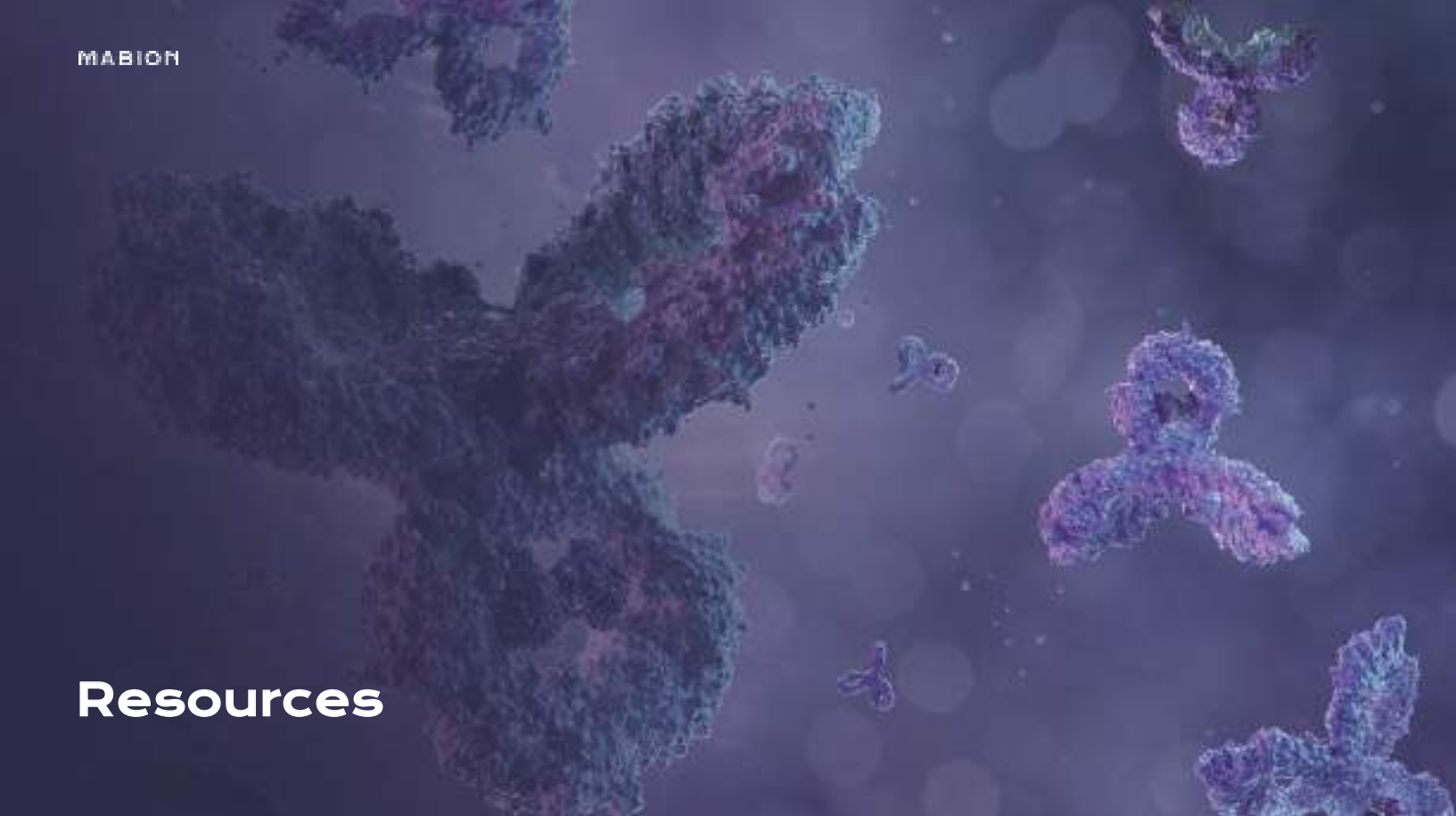
IV – Packaging and Serialisation

Packaging and Serialisation

Parameters	50 ml	10 ml	2 x 10ml
Unit package dimension [mm]	49,50 x 54,50 x 80,00	49,50 x 36,00 x 63,00	49,50 x 36,00 x 63,00
Box dimension[mm]	265,00 x 230,00 x 257,00	212,00 x 193,00 x 200,00	212,00 x 193,00 x 200,00
Quantity in the one case (box)	60 (60 vials)	60 (60 vials)	60 (120 vials)
Quantity of layers on a pallet	4 layers	4 layers	4 layers
Quantity of cases (boxes) on a pallet	36 cases (boxes)	80 cases (boxes)	80 cases (boxes)
Quantity of unit packages on a pallet	2160	4800	4800
Quantity of vials on a pallet	2160	4800	9600
Time of packaging + T&T Level 4	50 vials/min	50 vials/min	60 vials/min
Dimension of pallet	120 cm x 80 cm x 126 cm [length x widht x height]	120 cm x 80 cm x 104,80 cm [length x widht x height]	
Gross weight of pallet	258 kg	205 kg	378 kg



Resources

Contact

Mabion S.A.

SCIENTIFIC AND INDUSTRIAL COMPLEX FOR MEDICAL BIOTECHNOLOGY

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