MABION

Your End-to-End Biologics CDMO Partner

Clinical & Commercial Manufacturing

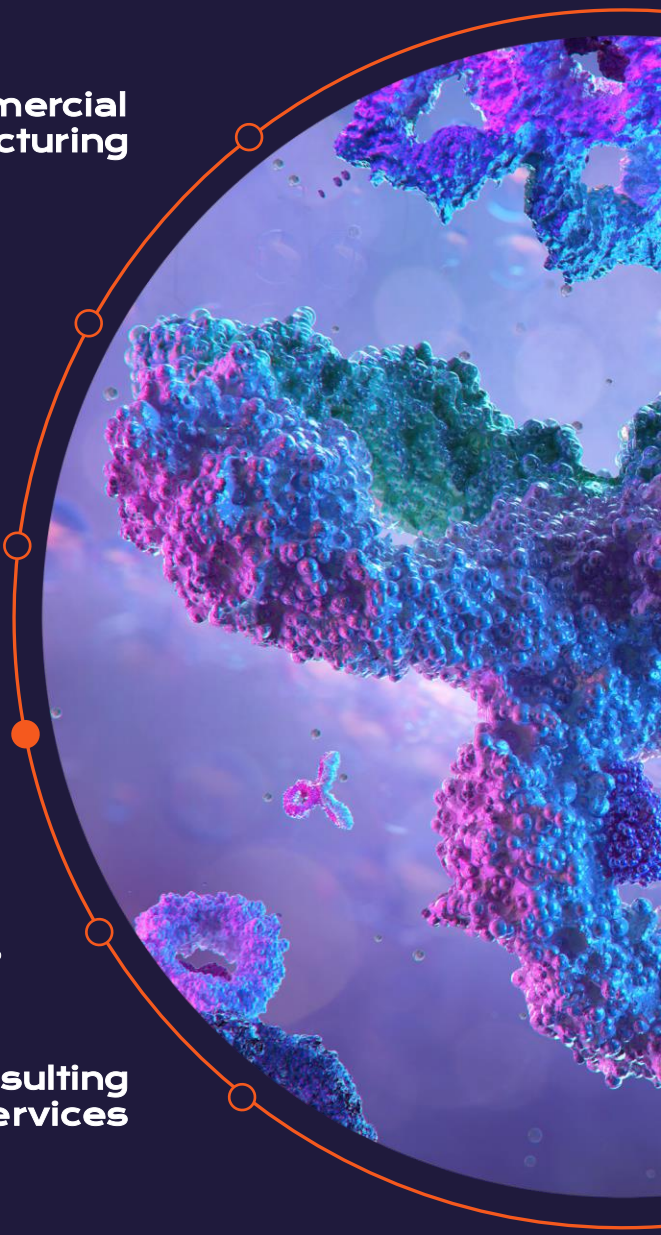
Fill & Finish

Process Development

Drug Characterization & Release Testing

Preclinical & Clinical Analytics

Regulatory & Consulting Services



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Executive Summary

- Mabion offers thorough analytical testing spanning early development, comprehensive state-of-the-art molecule characterization, QTPP, and biosimilarity studies (comparability and analytical similarity) as well as release/stability testing of clinical and commercial material (DS and/or DP).
- We cover the full method lifecycle, including method development and qualification/validation. Purity/impurities testing, advanced structural characterization using mass spectrometry, glycan analyses and multiple bioassays are all available in-house at Mabion either as a standalone service or as a support function for manufacturing operations.

We have expert knowledge of a wide range of molecules, such as monoclonal antibodies, antibody fragments, protein vaccine, ADCs and bispecific antibodies. We are flexible and focus on our customers' needs.

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About Our Company

- Mabion is an integrated biologic CDMO which is dedicated to the development and manufacturing of monoclonal antibodies, vaccine antigens and other biologics.
- Since its establishment in 2008, Mabion gained recognition as a comprehensive enterprise capable of performing top-quality end-to-end services related to the production of biologic drugs as well as their pre-clinical and clinical evaluation.
- Our key asset is the full-scale manufacturing facility containing multiple bioreactors of 200L and 2000L scale operated by highly skilled personnel with a thorough understanding of biologic drug production, analytics and regulations.
- What sets Mabion apart from most other CDMO's is its multidisciplinary character covering essentially all stages of biologic drug development starting from clone selection, through pre-clinical and clinical research, and ending with the marketing authorization process.

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About Our Company

- Our main GMP and ISO-certified manufacturing facility based in center of Poland, with multiple bioreactor lines of 200L and 2000L scale, is capable of producing biologic drugs and vaccine antigens in both clinical and commercial scale.
- Provided services include process development, transfer, scale-up and optimization as well as analysis and quality testing of the manufactured products.
- Our second facility located 20 minutes away, is dedicated to developing and performing pharmacokinetics, pharmacodynamics and immunogenicity assays for the purpose of pre-clinical and clinical research.

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About Our Drug Characterization and Release Testing Services

Molecule CQA Determination and Analytical Method Development

Method Qualification/GMP Validation/Transfer

Comprehensive Drug Characterization

(incl. comparability/similarity studies)

GMP Release and Stability Testing

Our expert team provides a continuous scientific, technical, quality and regulatory support throughout the entire biologic drug development process. We are your partner from the first stage of method development planning until routine release testing.

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About Our Drug Characterization and Release Testing Services

Molecule CQA Determination and Analytical Method Development

Mabion ensures regulatory compliance from the start by characterizing your molecule from the earliest stages of development. Mabion's specialist team can help your company achieve this goal through the following set of services:

- reviewing or determining Critical Quality Attributes (CQAs) of the developed molecule
- selecting adequate methods based on CQAs, stage of development, and purpose (Analytical Target Profile)– a risk-based approach
- using analytical quality by design (AQbD) tools to ensure that the method meets the desired quality attributes. These tools include analytical target profile (ATP), method operable design region (MODR), and method performance qualification (MPQ).
- developing customized, product-specific assays including identity by mass spectrometry or process-specific host cell protein assays
- developing assays using the DoE approach with appropriate statistical tools
- writing method standard operating procedures in accordance with GMP or Pharmaceutical Quality System requirements, including capture forms

ANALYTICAL METHOD DEVELOPMENT

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About Our Drug Characterization and Release Testing Services

Method Qualification/GMP Validation/Transfer

Understanding the uniqueness and inherent complexity of biologics, our expert team will help you adjust the validation or transfer testing to the current requirements of ICH, Ph. Eur., USP and other applicable guidelines.

Mabion team is ready to support your company in the following activities:

- design of the methods for drug analysis and qualification/validation which will be used for drug characterization, analytical comparability studies to support process changes as well as QTPP/similarity/comparative analytical assessment for biologic products
- comprehensive analysis of biologic molecules using developed and qualified/validated methods
- transferring analytical methods from third party laboratories for release/stability testing
- writing supporting documentation: qualification/validation/transfer protocols, capture forms and reports
- supporting the method lifecycle including method improvements and change implementation

ANALYTICAL METHOD QUALIFICATION / VALIDATION / TRANSFER

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About Our Drug Characterization and Release Testing Services

Comprehensive Drug Characterization

Mabion offers multilevel support in the analytical testing of biologics/biosimilars and vaccines across all development phases. Our expertise includes structural, physicochemical, and biological analyses.

Our dedicated team of experts can support you in the following activities:

- Characterization studies using selected methods or a full method panel for a given product, including mass spectrometry and bioassays
- Comparability studies supporting manufacturing process changes
- QTPP studies, including experience in reference product sourcing.
- Similarity/comparative analytical assessment studies for candidate biosimilars products
- Generation, characterization, and bridging of reference standards
- Stress/forced degradation testing in support of comparability/similarity studies
- Freezing stability studies
- Comprehensive mAb-based platform testing panel for lot release available to streamline implementation

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About Our Drug Characterization and Release Testing Services

Comprehensive Drug Characterization

DRUG CHARACTERIZATION / COMPARABILITY / SIMILARITY
METHOD PANEL

PHYSICOCHEMICAL ANALYTICS

- **PROTEIN CONCENTRATION** — ELISA, UV-VIS, HPLC-UV, HPLC-FLD
- **IDENTITY CONFIRMATION** — PEPTIDE MAPPING, WESTERN BLOT
- **MOLECULAR WEIGHT**
- **PROCESS-RELATED IMPURITIES** — ELISA, qPCR
- **PRODUCT-RELATED IMPURITIES** — CE, SEC, SDS-PAGE, WCX
- **GLYCOSYLATION PROFILE** — HILIC-UHPLC WITH MS, RP-HPLC-MS
- **MONOSACCHARIDE** — UHPLC-FLD
- **SITE OCCUPANCY** — UHPLC-FLD
- **OXIDATION, DEAMIDATION AND OTHER** — PEPTIDE MAPPING, MAPPING WITH MS
- **GLYCATION** — UHPLC-FLD

STRUCTURAL ANALYTICS

- **PROTEIN SEQUENCE CONFIRMATION** — UHPLC-MS, HPLCS-MS
- **DISULFIDE BRIDGES IDENTIFICATION** — UHPLC-MS
- **SECONDARY STRUCTURE** — CD
- **TERTIARY STRUCTURE** — CD
- **FREE THIOLS** — ELLMAN'S ASSAY

BIOLOGICAL ANALYTICS

- **CELL-BASED ASSAYS**
  - **CDC**
  - **ADCC** REPORTER AMD PBMC-BASED
  - **APOPTOSIS**
  - **ADCP**
- **PROTEIN-PROTEIN INTERACTION**
  - **SPR** FcR BINDING, FCRN, CD32, CD16
  - **ELISA**
  - **FLOW CYTOMETRY**
- **PROTEIN-PROTEIN INTERACTION**
  - **SPR** FcR BINDING, FCRN, CD32, CD16
  - **ELISA**

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About Our Drug Characterization and Release Testing Services

GMP Release and Stability Testing

Our GMP testing services span multiple assays to determine content, impurities, identity, purity, potency and excipients, including compendial assays. We offer custom-design studies compliant with ICH standards.

Specific services included in our portfolio are:

- Release testing of drug substance and drug product
- Testing of intermediate products / in-process pools as part of the control strategy
- Raw materials release testing
- QP release of drug product
- Stability testing
- Biosafety testing (Sterility/Bioburden, Mycoplasma, and Endotoxin testing)

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About Our Drug Characterization and Release Testing Services

GMP Release and Stability Testing

DRUG RELEASE TESTING
METHOD PANEL

PROTEIN CONTENT	PHYSICOCHEMICAL PROPERTIES	PRODUCT-RELATED IMPURITIES / VARIANTS / AGGREGATES	IN-PROCESS TESTING	PRIMARY STRUCTURE / IDENTITY	EXCIPIENTS	POTENCY	GLYCOSYLATION	PURITY / PROCESS RESIDUALS	DRUG-PRODUCT SPECIFIC
PROTEIN CONCENTRATION UV-VIS	APPEARANCE	SIZE-EXCLUSION CHROMATOGRAPHY SEC-HPLC	BACULOVIRUS TITER	PEPTIDE MAPPING LC-MS	POLYSORBATE CONTENT RSLC-UHPLC	ELISA	HILIC-UHPLC	PROTEIN A ELISA	VISIBLE PARTICLES
SPECIFIC PROTEIN CONCENTRATION ELISA	OSMOLALITY	ION-EXCHANGE CHROMATOGRAPHY WCX-HPLC	PROTEIN CONTENT BCA	POST-TRANSLATIONAL MODIFICATIONS	OLEIC ACID RP-HPLC	CELL-BASED BIOASSAYS ADCC, CDC		HOST-CELL PROTEIN ELISA incl. PROTEIN-SPECIFIC	SUB-VISIBLE PARTICLES
	pH	SDS-PAGE	PHOSPHATES	WESTERN BLOT				HOST-CELL DNA RT-PCR, PICO-GREEN	EXTRACTABLE VOLUMES
	CONDUCTIVITY	CAPPILARY ELECTROPHORESIS REDUCED AND NON-REDUCED						PLAQUE ASSAY	UNIFORMITY OF DOSAGE UNITS
								ENDOTOXIN LAL-GEL CLOT, TURBIDIMETRIC, CHROMOGENETIC	
								BIOBURDEN & STERILITY	
								MYCOPLASMA Q-PCR	

Industry Insights

Overview of Biologic Drug Regulations

- Although biological drugs are regulated similarly to standard medications, several important differences do exist and must be considered when planning the development program or preparing the regulatory dossier. Mabion understands the nuances of biological drug development and can turn this knowledge into a successful outcome.
- Specific guidelines applicable to biological drugs have been issued by both EMA and FDA. Knowledge of these guidelines and their practical implications is essential to the successful registration of a candidate product. Specialists from Mabion are there to help you with interpreting the most recent regulations and introducing them into your development framework.
- Pre-clinical and clinical development of biologics requires sophisticated bioanalytical methods that can reliably measure drug concentrations, pharmacodynamic profiles, and immunogenic potential of the developed molecule. Immunogenicity is an important parameter specific to biological drugs and vaccines, that receives particular attention from regulatory agencies. Pharmacologic characterization of your drug product will proceed with outstanding performance thanks to our well-equipped bioanalytical unit which cooperates closely with regulatory specialists.
- Biologics are much more sensitive to manufacturing process changes that frequently occur during drug development. Often, regulatory agencies expect additional evidence proving that these changes have not introduced any unintended effects into the molecule that could impact efficacy, safety or immunogenicity. Mabion Regulatory team can support you in identifying the need for additional data, discussing the comparability issues with regulators, and performing the required studies.

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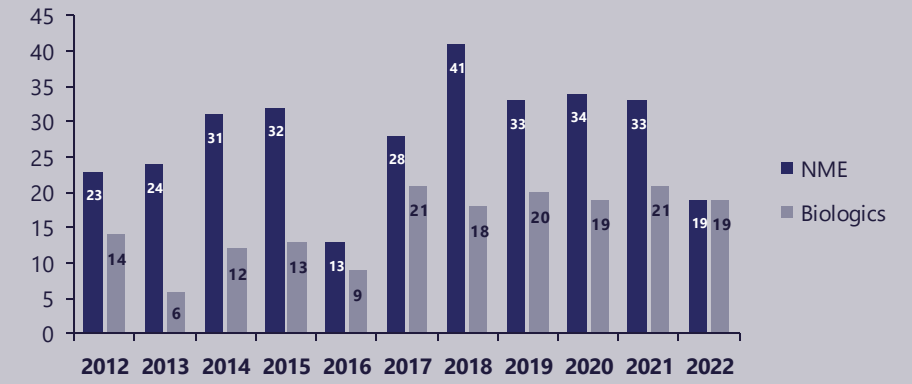
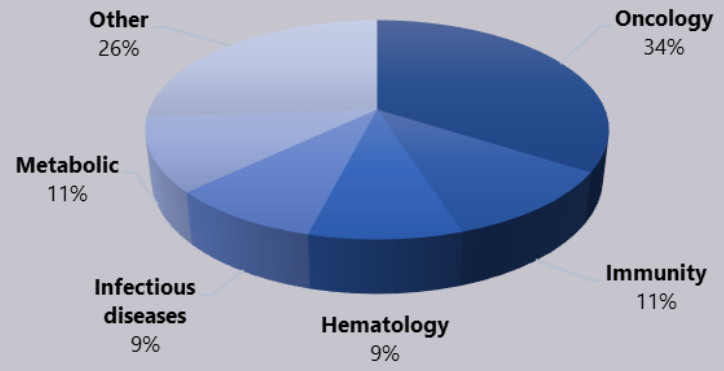
Industry Insights

- Between 2012 and 2021, FDA approved on average 44 drugs per year and the percentage of biologics among all approved drugs has risen steadily over the recent decades. In fact, in 2022, the number of new biologics entering the market has become equal to the number of approved small-molecule drugs. Most recent approvals were for oncology indications (34%) followed by immunity, metabolic, hematology and infectious diseases (9-11%).
- Much attention has been devoted to biosimilar drugs, which can be viewed as „generic" versions of the original biologics. Eighty-eight such products have been approved in the European Union and 40 in the US. Many more biosimilars are anticipated to enter the market within the next few years when more recently developed biologics go off-patent. It is hoped that the widespread use of biosimilars will increase patient access to novel therapies and limit healthcare spending.
- New innovative classes of biologics, such as bispecific antibodies, CAR-T, stem cells and gene therapies, are gaining momentum. Together they accounted for about half of biologic drug approvals in 2022, up from less than one-third in 2021.
- The total biologics market size is estimated at $366.36 billion in 2021[a] and is expected to rise significantly over the next years fueled by surging demand for new effective therapeutics. The market value in 2030 is predicted to reach $720 billion.
- Major players on biologics market are AbbVie, Johnson & Johnson, Amgen, Sanofi, Hoffmann-La Roche, GlaxoSmithKline, Novartis, Pfizer, Teva and CSL.

Biologic Drug Market



Number of FDA-approved drugs per year (all New Medical Entities and Biologics only)



Biologics approved by the FDA in 2022 by indication

[a] Source: *https://www.precedenceresearch.com/biologics-market*

Thank you for attention

Film presenting Mabion: https://youtu.be/Yb0MKDt-DJI

Mabion S.A.

SCIENTIFIC AND INDUSTRIAL COMPLEX FOR MEDICAL BIOTECHNOLOGY

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