MABION

Your End-to-End Biologics CDMO Partner

Clinical & Commercial Manufacturing

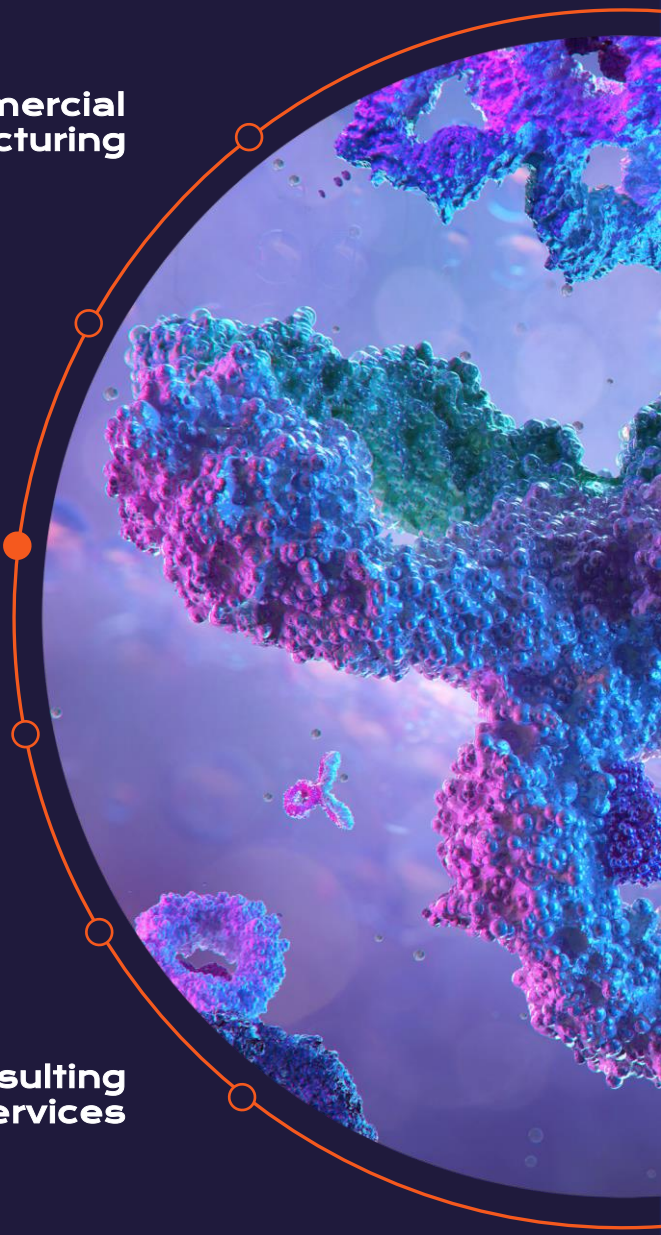
Fill & Finish

Process Development

Drug Characterization & Release Testing

Preclinical & Clinical Analytics

Regulatory & Consulting Services



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Executive Summary

- A robust, reproducible and well-controlled production process is key to success in the biopharmaceutical industry. This is why, we develop and constantly improve know-how that allows us to provide **professional and cost-effective services in process and analytical development**. The expertise of our team combined with state-of-the-art equipment and well-controlled quality management system enables us to implement customized solutions for projects of various complexity levels.
- Process development at Mabion includes the complex pathway from the **development of a stable cell line, through small-scale protein production and purification, to the design of a full-scale manufacturing process.** We have experience with both mammalian and insect cell lines, and the production of monoclonal antibodies and other recombinant proteins, but our approach to process development is always customized to the specific product and its unique characteristics.
- At Mabion, we know that implementation of the **Quality by Design** approach is the only way to guarantee a successful project outcome. That's why we start designing **fit-for-purpose analytical methods** starting from the earliest project phases and use them to control the successive phases of process development, and ultimately the process itself. This gives us a thorough understanding of the relationship between the process and the product, which leads to better control, more conscious development and scale-up as well as safe commercial production in the future.
- Our process development services include the **design of upstream, downstream and up-scale for processes**, including clonal evaluation and selection, culture media testing, protein purification and final product characterization. The key asset of our company is a strong analytical background, with multiple different methods available for use in process development and quality control

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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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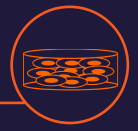
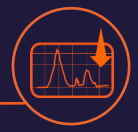
About Our Company

- 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.

About Our Process Development Services

- Clone Evaluation and Selection 
- Upstream Process 
- Downstream Process 
- Process Scale-up 
- Product Characterization 

In Mabion we appreciate the uniqueness of each biologic molecule. That's why, when designing a manufacturing process, we always pay close attention to the characteristics of each specific product, applying our broad experience and knowledge to every new project. Let us build the quality of your process from the start to guarantee successful drug development and approval!

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About Our Process Development Services

Quality by Design

The Quality by Design (QbD) framework is essential to improve and enhance the robustness of the biologics manufacturing process and the designing of analytical methods. The impact of QbD on the pharmaceutical industry has been reviewed in many publications, which stress the capabilities of this approach to increase the product quality, efficacy and safety. The concept of QbD is also applied to analytical methods, where the focus is on designing and developing methods that are robust, reliable, and provide accurate and precise results. Mabion implements QbD throughout the product and process development achieving outstanding productivity and quality of the manufactured products.

The QbD approach has a particularly high magnitude of benefits in the stage of product and process development and characterization, technology transfer, product and process monitoring and regulatory filings. These benefits include:

- For process development and characterization: operation at optimal conditions, greater flexibility and control, and increased knowledge on the molecule itself;
- For technology transfer: reduction in risk of failure or delays;
- For process monitoring and regulatory filings: quality assurance during product lifecycle.

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About Our Process Development Services

Comprehensive Drug Characterization

In the process of derivation of cell lines producing therapeutic proteins, it is extremely important that the line is monoclonal, stable, highly productive and that the resulting product has a quality profile that is consistent with expectations.

Both experience and knowledge as well as the right equipment are crucial to secure a successful outcome. Our scientists always use high-throughput systems to complete the process of clonal selection of cells from heterogeneous populations.

Thanks to the combination of knowledge and technology, we can select the clones with the highest productivity, which is one of the most important attributes for industrial applications.

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About Our Process Development Services

Upstream Process

Our offer includes the full design of the upstream manufacturing process, from clone selection through optimization of the culture conditions and ending with the efficient expression of the desired product.

The most important services provided by Mabion are:

- Derivation of the stable/transient cell line
- Clone stability testing
- Production and testing of research cell banks
- Optimization of cell culture at lab scale (from 10 ml to 10L)
- Small-scale process characterization and scale-down validation studies

About Our Process Development Services

Upstream Process

Culture Media Testing

During the development of culture conditions for antibody-producing cells, testing the levels of nutrients in the culture media and metabolites secreted by the cells during culture plays an important role.

For this purpose, we use fully automated, high-throughput equipment that allows us to perform several hundred tests within a few hours. The analysis of the content of culture fluid components is performed based on enzymatic reactions and colorimetric measurements. Using this data, we can choose appropriate conditions for cell supplementation to increase the efficiency of the culture and improve the quality of the obtained product. We also monitor the content of metabolites that may have a negative impact on cell growth and viability.

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About Our Process Development Services

Downstream Process

Following the development of the upstream process, our team of specialists provides the best solutions for downstream processing. In our work, we always adopt a holistic approach, viewing the entire manufacturing process as a complex interplay of many factors functioning at different stages of production. This approach guarantees the development of a reproducible, reliable and efficient process that can meet all regulatory expectations.

Among our services related to the downstream process development one can find:

- Harvesting (through depth-filtration and centrifugation)
- Viral inactivation and clearance
- Protein concentration (normal and tangential flow filtration) and buffer exchange
- Protein purification using various chromatography techniques (from 1mL to 100mL)
- Small-scale process characterization and scale-down validation studies

About Our Process Development Services

Downstream Process

Protein purification

In the development of the purification process, we use state-of-the-art lab-scale systems that have their counterparts on an industrial scale. We use these lab-scale systems to develop purification methods, as well as to optimize the existing ones.

We use advanced, specialized software that is tailored to our process equipment for the design of experiments (DoE) as well as their control. Our attention to experimental work results in the high performance of the processes we develop.

Thanks to the appropriate design and software, our devices ensure control over the process conditions, as well as their proper monitoring and data archiving. Additionally, we can simulate the future course of processes on a laboratory scale-down models to the smallest detail. This reduces the time of process implementation as well as the cost of transfer.

About Our Process Development Services

Process Scale-Up

Our multidisciplinary team performs scale-up from the laboratory level, through the scale of 200L - 250L (if required), to the full commercial scale of 2000-2500L. The entire process is done with thoughtful consideration of the EMA and FDA guidelines (incl. FDA 21 CFR Part 11 standards) as well as the outcomes of our clients' interactions with regulatory agencies.

Scale-up process performed by Mabion includes the following stages:

- Determination of critical product quality attributes (CQAs), critical process parameters (CPPs) and key process parameters (KPPs).
- Determination of acceptance criteria (PAR – Proven Acceptable Range, NOR – Normal Operating Range) for individual process parameters.
- Process characterization and determination of the process space for individual stages of drug product manufacturing (SDM, OFAT, QbD).
- Testing the purity, quality and stability of active substances and finished products.

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About Our Process Development Services

Product Characterization

In order to prove that the obtained product has the appropriate quality characteristics, we perform several physicochemical and biological analyses. Together they allow for a comprehensive structural and functional characterization of protein products.

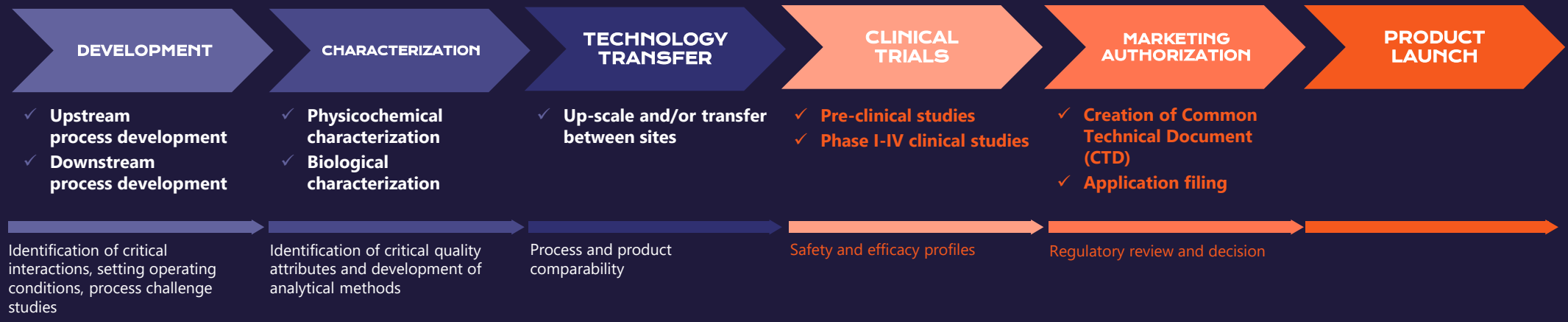
Deep understanding of protein analytics gained through extensive experience with cutting-edge analytical systems, allows us to develop, optimize, qualify, and validate high-quality analytical methods that satisfy all requirements of regulatory agencies. Analyses that can be performed by Mabion include:

- Evaluation of critical protein quality attributes (e.g., glycosylation, aggregates) using modern high-performance liquid chromatographies (HPLC, UHPLC). UHPLC system is equipped with three types of detectors: UV-VIS, fluorescence and corona discharge. One of the systems is also coupled to MS.
- Determination of amino acid sequence and post-translational modifications (using MS and other methods)
- Determination of protein purity (using capillary electrophoresis with modular UV-VIS and LIF detectors that can be integrated with MS)
- Measurement of interactions between molecules, incl. affinity and association/dissociation constants (using state-of-art SPR technology)

Industry Insights

Development stages

All product development stages presented below are covered by Mabion's offer.



Industry Overview

- The outsourcing of biological drug development has been growing in recent years, particularly following the outbreak of COVID-19 pandemic, which required immediate production of massive amounts of vaccine antigens and antiviral monoclonal antibodies. As many as 230 agreements have been signed for this purpose between vaccine or drug developers and various CDMOs. **One of these agreements was signed between Mabion and Novavax, governing the production of rS spike protein – the main ingredient of COVID-19 vaccine sold under the brand name of Nuvaxovid.**
- However, the trend to increase outsourcing had been already present before the pandemic, fueled by small bio-tech enterprises that must rely on external companies to manufacture their candidate products for research purposes. All these developments created a very challenging situation for CDMOs, in which the products had to be produced and delivered at unprecedented speed.
- The number of biological drug approvals in the US has been also increasing over the recent decade. The biopharma industry has witnessed the arrival of new classes of drugs and innovative treatments such as cell and gene therapies, bispecific antibodies or antibody-drug conjugates. **Mabion, with its highly qualified staff and cutting-edge technologies, is ready to respond to these new demands and work with any partner that plans to develop manufacturing process for the novel or biosimilar therapeutic modalities.**
- COVID-19 pandemic has once again illustrated the importance of manufacturing flexibility and the requirement for high speed to market. Delays in development are currently most often caused by supply shortages and inability to quickly transfer projects between different sites. **Mabion has an excellent record of hitting project deadlines both in sourcing raw materials and performing the technology transfer. A fine example of this process is the incredibly quick installation of the new expression system at Mabion, involving Sf9 insect cell line, and associated processes required for manufacturing of the Novavax vaccine.**

Key challenges for manufacturers

137

new biologics approved by FDA in the last decade

230

*agreements signed between the developers of COVID-19 vaccines or therapies and CDMOs**

* The number concerns publicly disclosed agreements signed until January 2022

Thank you for attention

Film presenting Mabion: https://youtu.be/2hzQI5ZGyxk

Mabion S.A.

SCIENTIFIC AND INDUSTRIAL COMPLEX FOR MEDICAL BIOTECHNOLOGY

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