Customized Biomaterials

Development & Manufacturing

Living Immunoassay
Excellence

werfen

Werfen is a growing, family-owned, innovative company founded in 1966 in Barcelona, Spain.

Our OEM Technology Center has consolidated experience in research, development and manufacturing of customized assays and biomaterials.

We offer end-to-end solutions for the IVD industry with the most innovative capabilities to enhance competitiveness and time-to-market.

Our mission is to become your partner of choice as a center of excellence in providing innovative end-to-end OEM solutions (products & services) to IVD companies.

Innovation

Our OEM Technology Center ranks among the top centers of excellence for immunoassay and biomaterial development and manufacturing in the industry. Our focus on technological advances ensures our customers access to state-of-the-art R&D and manufacturing capabilities. Werfen's innovative nature is strengthened through close relationships with prestigious universities and biotechnology research centers around the world.

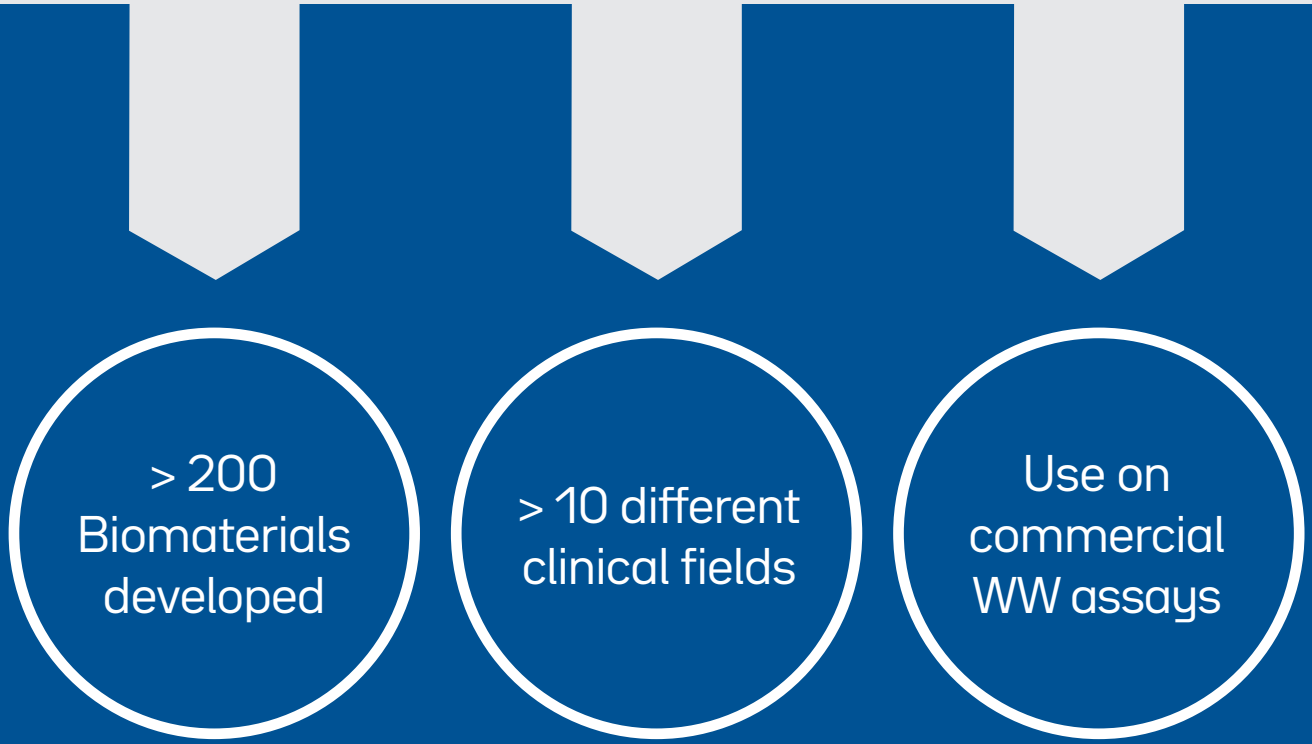
Operational Excellence

Our key strength is the combination of the ongoing effort to improve our organizational processes, products and services with the Werfen mindset that embraces principles and tools to create a sustainable partnership with our customers and employees.
Our Quality System is certified to ISO 13485:2016 / EN ISO 13485:2016 as well as MDSAP.

Commitment

Customers and patients benefit from the efficiency of a talented global team of qualified and specialized professionals who lend their enthusiasm, dedication and energy on a daily basis in order to provide high quality products & services.

You can rely on the expertise and capabilities of our R&D and Operations teams to develop and manufacture customized Biomaterials



What can Customized Biomaterials offer you?

Antibody & Antigen *de novo*: Design, Development and Manufacturing

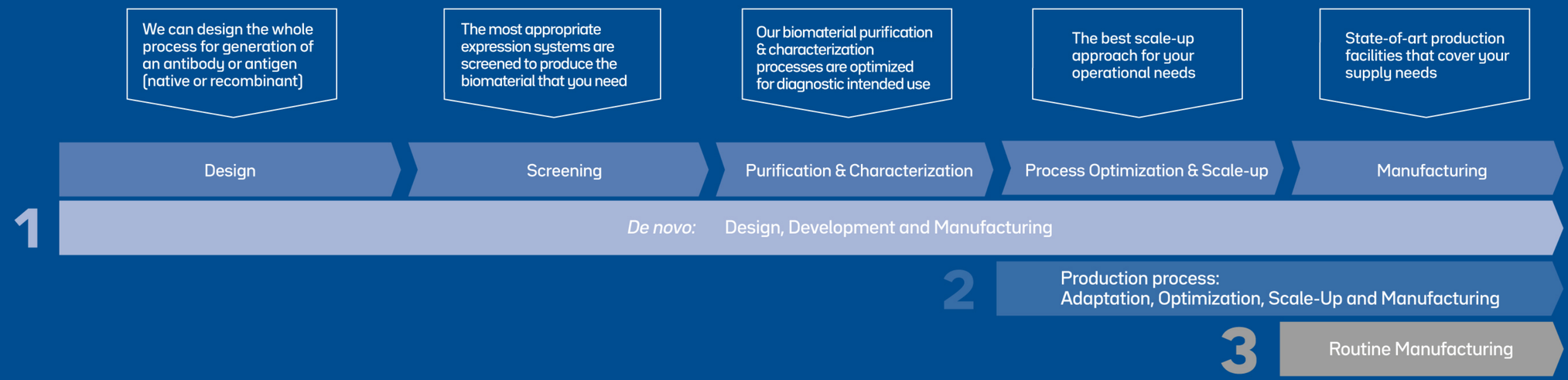
Develop from inception of a biomaterial for diagnostics, from new antibody or antigen selection to routine production processes, adapted to your operational demands.

Antibody & Antigen production process: Adaptation, Optimization, Scale-up and Manufacturing

Improve the production yield and/or performance of your biomaterial of interest.

Antibody & Antigen Scale-up and Manufacturing

Optimize your daily operations and meet demand increases thanks to our biomaterial production capabilities.



Design

Based on your needs we can design the entire process for generating a new recombinant antibody.

If you already have an antibody in mind, we can modify it to meet your needs: improving affinity, sequence modification, tag addition, etc. Our expertise in recombinant antibodies extends to different antibody formats. If your needs are related to a specific antigen, we can also design the entire generation and production process for this new recombinant antigen or we can modify an existing one by improving affinity, sequence modification, tag addition, improving stability, among others. In addition, we have in-house bioinformatics protein modelling to simulate how the biomateiral could be affected in different conditions.

One of the major challenges for an IVD company is to obtain IgM-positive plasma and serum to be used as controls or calibrators for diagnostic assays since IgMs have a short life, disappearing earlier than IgGs. In order to overcome this challenge, our customized biomaterials team has developed a process to generate a recombinant IgM antibody that can be used as a calibrator or control for a diagnostic assay.

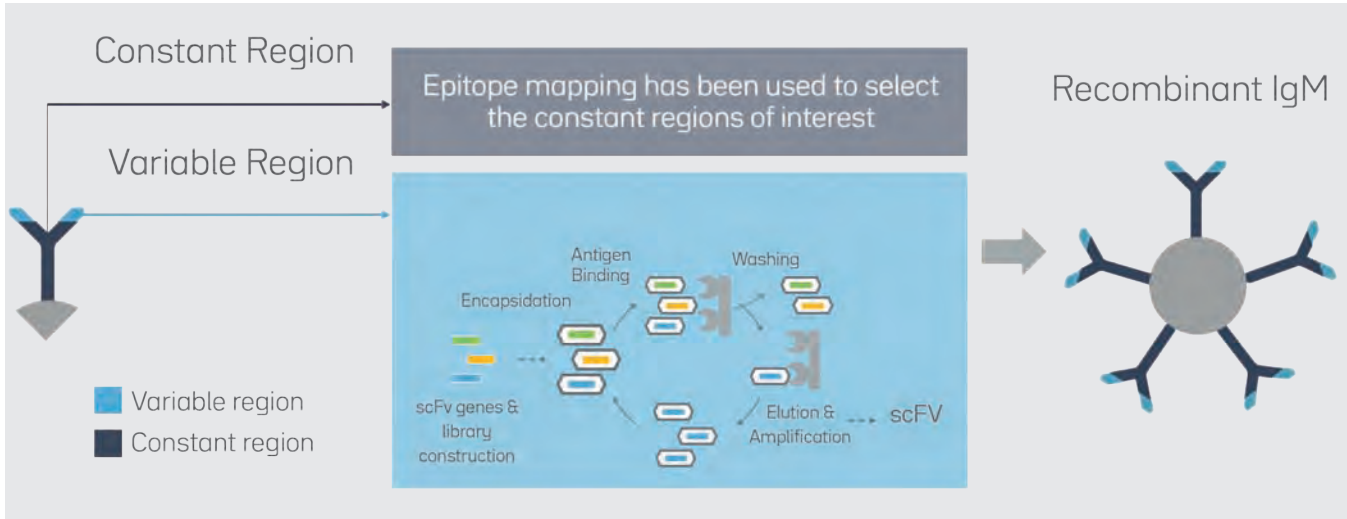


Figure 1. Summary of the process of generating an IgM antibody to be used as a calibrator or control

Screening

In this step of the process, the most appropriate expression systems are screened based on production yield, protein performance, stability, binding kinetics and cell viability.

At the end of the screening step we can select the ideal strain/clone that would produce the biomaterial that will best meet your needs.

Our current R&D expertise and our current operations use the following biomaterial sources to produce the biomaterials needed to supply assays covering a wide range of clinical fields to customers worldwide.

Microbial strains: Recombinant antigens

Hybridoma cell lines: Monoclonal antibodies against viral & human antigens

Mammalian cell lines: Viral & human antigens

Baculovirus expression systems: Viral & human antigens

Native: Viral, human & mammalian antigens. Polyclonal antibodies

Yeast: Recombinant antibodies & antigens

Purification & Characterization

Our extraction & purification platforms are optimized taking in consideration that the purified antibody/protein will be used in a diagnostic assay. Based on your needs, we can perform peptide mapping analysis, evaluate state of aggregation, as well as determining your sample molecular weight distribution, purity, charge variants and glycosylation patterns among others.

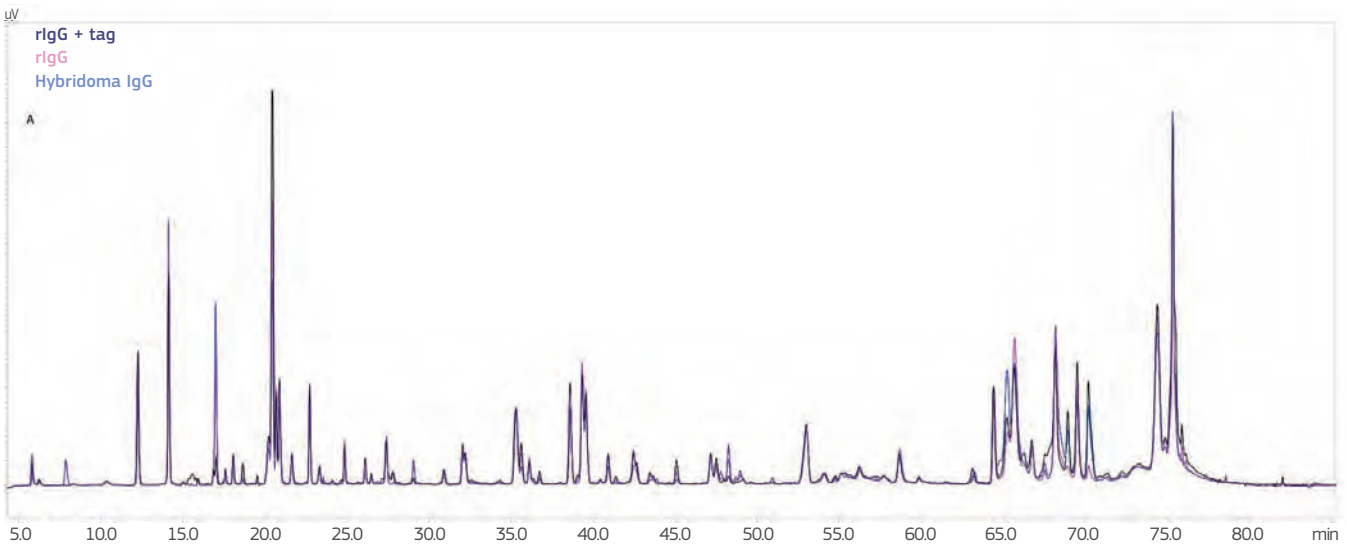


Figure 2. Example of Peptide Mapping (PEM).

The characterization process of biomaterials to be used in diagnostic products is key to understanding and managing posttranslational modification variants, along with process and product related impurities. This approach is crucial for product consistency and quality. One of our customers requested that our customized biomaterials team characterize a full IgG antibody from hybridoma, and a new recombinant IgG antibody (designed as an alternative for the full IgG antibody from hybridoma). As you can see in Figure 2, the peptide mapping done by our customized biomaterials team ensured that both the hybridoma and recombinant IgG molecules ultimately presented a similar tryptic profile.

During the process of producing an antibody, the glycosylation pattern must be understood in order to assess the performance and reproducibility of the selected antibody. Our biomaterials team did the analysis of the glycosylation pattern (Figure 3) of a full IgG monoclonal antibody and a F(ab')2 fragment from the same hybridoma. The objective of this analysis was to optimize the cell culture and the purification conditions of that monoclonal antibody and its F(ab')2 fragment.

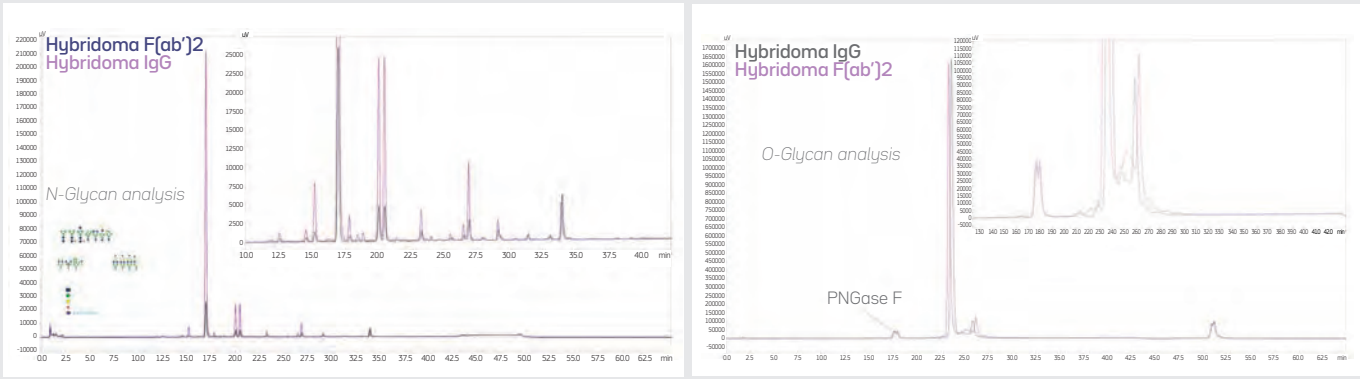


Figure 3. Example of Hydrophilic Interaction Chromatography (HILIC) to assess glycosylation pattern.

Moreover, functional tests for the requested biomaterial can be provided. These tests include affinity constants and interaction kinetics by biolayer interferogram and surface plasmon resonance as well as diagnostic assays.

Apart from Bio-Layer interferometry and surface plasmon resonance, our biomaterials can benefit from R&D assay development to assess the functionality of a new biomaterial in latex based or chemiluminiscence based immunoassays.

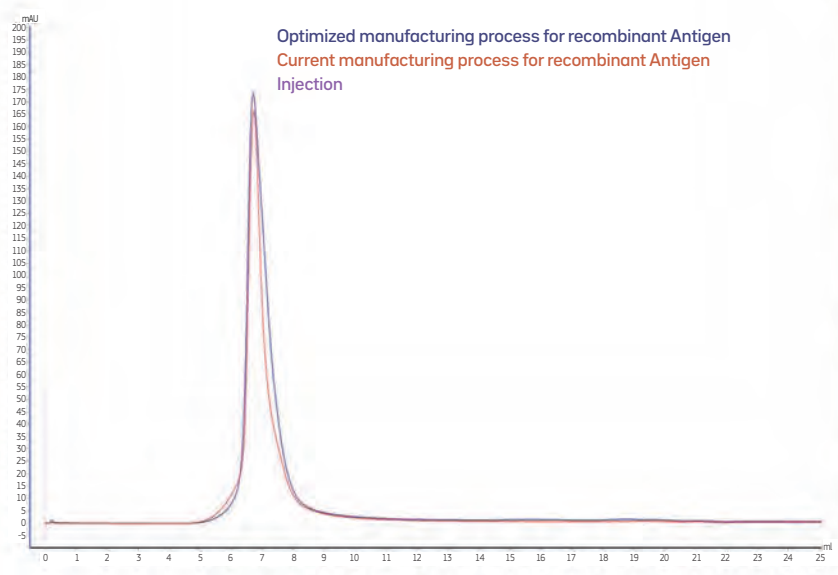
Process Optimization & Scale-up

The strategy for process scale up is selected based on your operational demands. When scaling up, an optimization process is needed in order to improve productivity and streamline supply chain operations.

When facing a production process optimization and scale-up, our biomaterials team (a co-team of biotecnhology R&D and Manufacturing) takes into consideration the improvement of the protein or antibody expression system and optimization of the culture conditions to increase the specific production of the biomaterial for diagnostics.

Once the production process is optimized it can be scaled up to the optimal production system such as a bioreactor up to 100L.

Our biomaterials team works towards the goal of streamlining biomaterials production so as to optimize and scale up the production process for a biomaterial for diagnostics. In figure 4 you can see a couple of examples of the results obtained after the manufacturing process optimization and scale-up to bioreactior of a recombinant viral antigen (virus like particles) to be used for a diagnostic assay to detect antibodies.



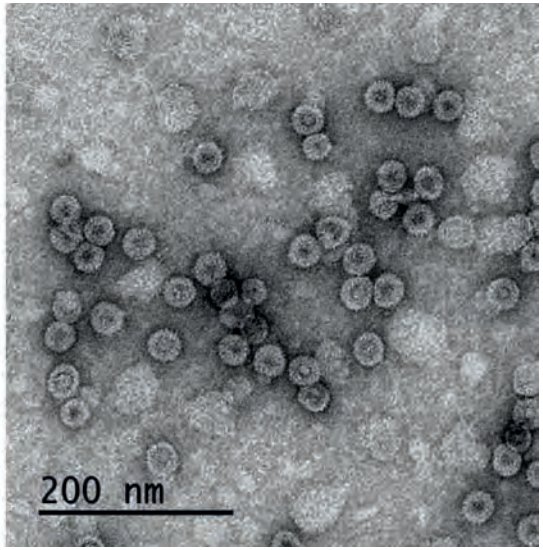


Figure 4. Example of a manufacturing processs optimization and scale-up: In the graph on left Size Exclusion Chromatography for the analysis of the recombinant antigens obtained with curent and optimized manufacturing proceprocess and a electronic microscopy image of the recombiant antigens obtained after the manufacturing process optimization and scale-up.

Manufacturing

Werfen's state-of-the-art production facilities can adapt to your supply needs thanks to their capabilities:

We have the biomaterial supply chain integrated in the same building, this allows us to being able to secure the supply to our partners. Note that in the midst of the 2020 WW health crisis, during the first half of the year we were able to supply more than 20 different Biomaterial references to more than 15 different IVD companies located worldwide.

- 35,000 m^2 (376,736 ft^2) facilities, including 9,200 m^2 (99,000 ft^2) dedicated to production activities
- State-of-the-art equipment: Bioreactors, AKTA Systems among others
- More than 200 product dedicated purification columns
- Positive-and negative-pressure laboratories
- Biosafety level 2 laboratories
- Production under GMP procedures
- Final QC, physicochemical and functional analysis

With Werfen's Customized Biomaterials you can get access to

Upstream Capabilities

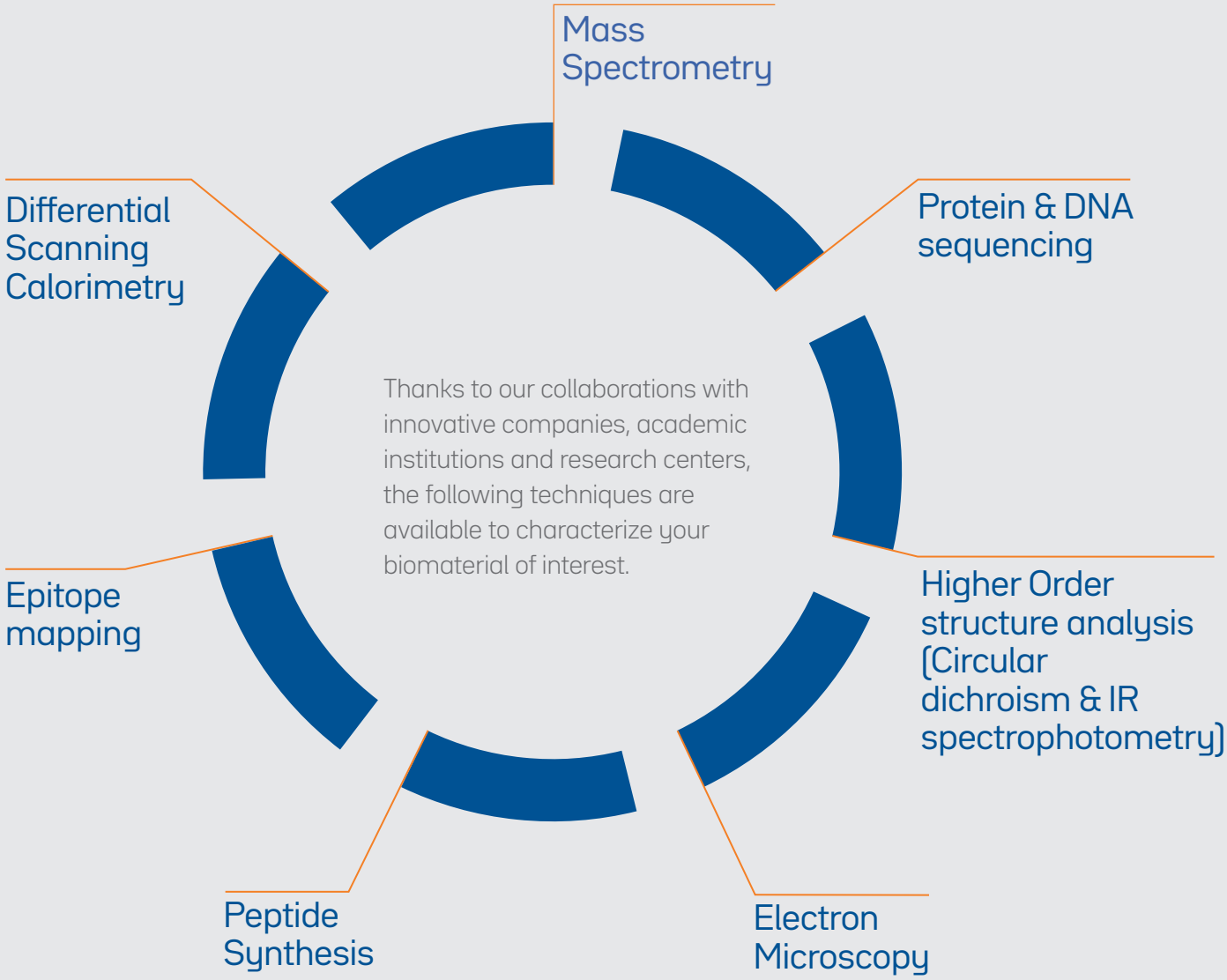
Biomaterial Sources			
Monoclonal Antibodies	**Polyclonal Antibodies**	**Native Antigens**	**Recombinant Proteins**
Hybridorna Cell Lines	Goat	Bacteria	Microbial Strains
Mammalian cell lines (recAb)	Rabbit	Viruses	Mammalian Cell Lines
	Guinea Pig	Human Sera	Baculovirus Expression System
			Yeast

In-Process Controls
Viable and total cells concentration by automatic cell counter
Nutrients and byproducts analysis
Cell population analysis
Cell culture aminoacid analysis

Downstream Capabilities

Protein Purification
Protein Extraction
Centrifugation & Ultracentrifugation
Microfiltration & Ultrafiltration
Chromatography (Affinity, IEX, SEC, HIC, Multimodal)
Protein refolding
Chemical modification
Labeling

Protein Characterization	
Physicochemical Analysis	**Functional Analysis**
UV Spectrophotometry	Surface plasmon resonance
Electrophoresis	Bio-Layer Interferometry
Isoelectric point determination	Enzyme-Linked Immunosorbent Assay (ELISA)
Ion exchange chromatography	
Glycosytation pattern	
Peptide mapping	Chemilluminescent Immunoassay
Protein amino acid analysis	
Surface hydrophobicity	
DSF (differential scanning fluorimetry)	Latex based immunoassay



Our facilities are located in Llicà d'Amunt, Barcelona and cover more than 35,000 m^2 (376,736 ft^2). Contact us at OEM@werfen.com to discuss your customized Biomaterial needs and request a call back.

Living Immunoassay Excellence

werfen

Can Malé
08186 Lliçà d'Amunt
Barcelona, Spain
Phone: +34-93-860-9000
werfen.com/oem

3100-9803 R01 SEPTEMBER-2021