Customized Biomaterials

101

Development & Manufacturing

Living Immunoassay Excellence



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.

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



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

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 oppropriate 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/clane 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.



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 biornoterials to be used in diagnostic products is key to understanding and managing postiransiational 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 biomoterials team characterize a full IgG antitadu from hybridoma, and a new recombinant IgG antibody (designed as an atternative for the full IgG antibody from hybridoma). As you can see in Figure 2, the peptide mapping dane by our customized biomaterials team ensured that both the hybridama and recombinant IgG malecules uttimately presented a similar truptic 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.



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, on 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 MD companies located worldwide.

- 35,000 m² [376,736 ft²] facilities, including 9,200 m² (99,000 ft²) dedicated to production activities
- State-of-the-ort equipment: Bioreactors, AKTA Systems among others
- More than 200 product dedicated purification columns
- Positive-and negative-pressure laboratories
- Biosofiety leval 2 laboratories
- Production under GMP procedures
- Final QC, physicochemical and functional analysis

With Werfen's Customized Biomaterials you can get access to

Upstream Capabilities

Downstream Capabilities

Biomaterial Sources					In-Process Controls	
Monoclonal Antibodies	Polyclonal Antibodies	Native Antigens	Recombinar Proteins	nt	Viable and total cells concentration by	
Hybridorna Cell Lines	Goat	Bacteria	Microbial Strains Mammalian Cell Lines		Nutrients and byproducts analysis	
Mammalian cell lines (recAb)	Baculovirus Expression System					
			Guinea Pig	Human Sera	Cell culture aminoacid	
	Yeast				analysis	
Protein Purification Protein Characterization						
Protein Extraction		Physicochemical Analysis		Functional Analysis		
Centrifugation & Ultracentrifugation		UV Spectrophotometry		Surface plasmon resonance		
		Electrophoresis		Bio-Lauer Interferometru		
Microfiltration & Ultrafiltration		Isoelectric point determination				
Chromatography (Affinity, IEX, SEC, HIC, Multimodal)		lon exchange chromatography		Enzy	Enzyme-Linked	
		Glycosytation pattern		Immunosorbent Assay (ELISA)		
Protein refolding		Peptide mapping		Chemilluminescent Immunoassay		
		Protein amino acid analysis				
Chemical modification		Surface hydrophobicity				
Labeling		DSF (differential scanning fluorimetry)		Late>	based immunoassay	



Our facilities are located in Llicà d'Amunt, Barcelona and cover more than 35,000 m² [376,736 ft²]. Contact us at OEM@werfen.com to discuss your customized Biomaterial needs and request a call back.

Living Immunoassay Excellence

11



Av. Can Montcau, 7 08186 Lliçà d'Amunt Barcelona, Spain Phone: +34-93-860-9000 werfen.com/oem