



Biopharmaceutical Services



Monoclonal antibodies are large molecules that comprise of hundreds of amino acids in addition to post-translational modifications. Elucidating the structure and functionality of these proteins is difficult but necessary for regulatory submissions. To develop therapeutic monoclonal antibodies, it is mandatory to conduct analytical studies, which must be tightly bound to production process control, since any change in any step of the process may modify the structure, hence the assertion that, the process is the product in biologic field.

Curaxys is specialized in the development of any monoclonal antibody, being able to carry out a complete process from the generation of the cell line that produces the target protein, to the physico-chemical characterization.

For those companies working to develop therapeutics monoclonal antibodies, Curaxys offers a complete package service, including analytical-bioanalytical assays and the production of the product to perform the preclinical characterization.

Main areas of expertise:

1. Proof-of-concept of new molecules.
2. Development of preclinical characterization (full-service).
3. Development of production- and purification integrated process.
4. Production of biomolecules for preclinical assays.



Cell line development:

Designing and subcloning of expression vectors for the production of recombinant proteins in prokaryotic or eukaryotic cells (Amaxa 4D-Nucleofector; Bio-Rad Gene Pulser Xcell).

Generation of cell lines to produce any recombinant protein/peptide, by means of transfection either by electroporation or nucleofection and gene silencing preventing systems (Amaxa nucleofector; Biorad Gene Pulser).

Development and selection of cell lines from stable clones, hence significantly reducing the standard timelines available in the market so far, by means of automated hi-tech to select those clones, which display the highest yields (Clonepix 2 System, Molecular Devices).

Upstream process:

Development and optimization of production process using 2L bioreactors specially equipped for fed-batch and perfusion process (Bioreactores Biostat B plus, Sartorius, ATF2-H Refine technology, Vicell XR Beckman Coulter, Rapidlab 348, Siemens).

Establishment and optimization of cell lines culture conditions and parameters using high output technologies (Minibioreactores Micro24 reactor, Pall, Vicell XR, Beckman Coulter, Rapidlab 348, Siemens).

Optimization of cell culture and production of recombinant proteins with different combinations of culture media and supplements (Minibioreactores Micro24 reactor, Pall, Vicell XR Beckman Coulter, Rapidlab 348, Siemens).

Downstream process:

Optimization and development of chromatography single-steps and purification whole process, with FPLC purification devices (AKTA Avant).

Optimization of TFF (Tangencial Flow Filtration) process (Sartoflow Slice 200).

Optimization of depth filtration process by Pmax method.

Analysis of impurities:

- Host cell DNA, by qPCR (quantitative polymerase chain reaction) (ECO real time PCR, Illumina).
- Host cell proteins by ELISA (Enzyme-linked immunosorbent assay) (Varioskan Flash Spectral, Thermo Scientific).
- Quantification of protein A leakage by ELISA (Enzyme-linked immunosorbent assay) (Varioskan Flash Spectral, Thermo Scientific).

Protein characterization:

Charge Heterogeneity by IEX-HPLC. (HPLC, Hitachi LaChrom ELITE).

Protein quantification (HPLC, Hitachi LaChrom ELITE/ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).

Determination of mass intact. (ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).

Peptide mapping. (ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).

Post-translational modifications:

- N-Linked oligosaccharide profiling (ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).



- o Glycan content (ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).
- o Oxidations and deamidations of aminoacids (ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).
- o Disulfide bridges and free cysteine analysis.

N- and C-terminal sequencing.

Amino acid compositions analysis (ACQUITY UPLC H-Class Bio System-Xevo G2-S QTof).

Aggregation analysis (SEC-HPLC, Hitachi LaChrom ELITE).

Misfolding analysis (RP-HPLC, SEC-HPLC, Hitachi LaChrom ELITE).

Western blot.

SDS-PAGE.

In vitro Bioassays:

Ligand binding assays (FACScalibur™ flow cytometer, BD Bioscience. ProteOn™, BioRad).

Fc gamma receptor binding assays (FACScalibur™ flow cytometer, BD Bioscience. SPR ProteOn™, BioRad).

Cell proliferation assays (FACScalibur™ flow cytometer, BD Bioscience)

Neutralization assays

Potency assays

Mode of action: ADCC (Antibody-Dependent Cell-mediated Cytotoxicity) (FACScalibur™ flow cytometer, BD Bioscience), CDC (Complement-dependent cytotoxicity) (FACScalibur™ flow cytometer, BD Bioscience).

Development:

For those clients who wish to save in-house resources, Curaxys offers a full service package including evaluation of candidate products for assessment and to determine which ones to take forward to further studies, as well as assay design development and validation, and efficacy testing. For further customized services, please, do not hesitate to contact us.



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