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Program Overview: Anti-CD20 Antibodies
Example: Rituximab

Project Package

- Physicochemistry/structure
- Function/comparability – biological activity assays
- Formulation
- Biosimilar nonclinical *in vivo* package
- Biosimilar preclinical/clinical laboratory support package
- Lot release and stability testing

Charles River has a range of services to support our clients' biosimilar development programs, from GMP facilities for performing characterization and lot release testing through *in vivo* preclinical studies and support assays for both preclinical and clinical sample analysis. Combining the experience across the company, we have developed a comprehensive program that clients can use to support the development of anti-CD20 monoclonal antibodies.

The Goal

Biosimilarity is one of the key aspects that a company must pursue during the development of a biosimilar product. Proving biosimilarity along with efficacy and safety of their therapeutic provides a compelling case for approval under the regulations governing biosimilar market authorizations. When companies find structural and functional differences, it is essential that they prove these differences do not impact the clinical safety and efficacy on file for the innovator product. In some cases, the complexity of biosimilars make their development journey much longer and more expensive than their generic counterparts. The key to success with a biosimilar is being first to market, and to do this clients need an experienced partner who has worked with the originators and already has in place the institutional knowledge, subject matter experts, and assays needed to accelerate development.

Supporting Our Clients' Programs

We collaborate with our clients in their biosimilar development programs from *in vivo* preclinical studies and support assays for both preclinical and clinical sample analysis through GMP facilities for performing cell banking, cell line/product characterization, and lot release testing. As a global company with expansive scientific expertise and the experience of working with a multitude of originator and biosimilar compounds, we guide clients from discovery to approval and provide continuity for their entire program. This means that they can work with one provider instead of investing time and money qualifying multiple vendors.

Navigating the regulatory landscape is also key to being first to market. Our scientific advisory services group is able to efficiently guide clients through the many guidelines aimed specifically at the development of biosimilars.

EVERY STEP OF THE WAY

The program outline below is based on the class of drug, scientific experience, and published guidance documents.

Biosimilar Characterization Package	
Physicochemistry/Structure	**Function/Comparability – Biological Activity Assays**
Protein quantity and purity	Antibody-dependent cell-mediated cytotoxicity (ADCC) assay
Molecular weight determination by MS	Complement-dependent cytotoxicity (CDC) assay
Amino acid sequence by LC-MS/MS and Edman degradation	Antibody-dependent cellular phagocytosis (ADCP) assay
Glycosylation and other PTMs analysis	Apoptosis assay
Physicochemical properties	Flow cytometry binding assay
Aggregation analysis by SEC-MALS and AUC	Fc receptor assays
	In vitro biocomparability
Biosimilar Nonclinical *In Vivo* Package	**Biosimilar Preclinical/Clinical Laboratory Support Package**
Pharmacology/pharmacodynamic PK/PD study	Bioanalysis and pharmacokinetic (PK) analysis
4-week comparative toxicity study	Immunogenicity
Tissue cross-reactivity	Pharmacodynamic (PD) endpoints (e.g., immunophenotyping)
	Neutralizing antibody assays
Formulation	**Lot Release and Stability Testing**
Preformulation	Pilot study
Stress studies	Release/stability methods development and validation
Product formulation (or reformulation)	Routine testing
	Stability testing including accelerated stress condition testing with mode of action assays