charles river

Program Overview: Anti-TNFα Monoclonal Antibodies

Examples: Etanercept (fusion protein), Adalimumab, and Infliximab

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

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 the therapeutic provides a compelling case for approval under the regulations governing biosimilar market authorizations. When structural and functional differences are noted it is essential that companies 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 starting from *in vivo* preclinical studies and support assays for both preclinical and clinical sample analysis through to 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.

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**
Extinction coefficient	Antibody-dependent cell mediated cytotoxicity (ADCC) assay
Protein quantity and purity	Complement-dependent cytotoxicity (CDC) assay
Process and product-related impurities analysis	Antibody-dependent cellular phagocytosis (ADCP) assay
Amino acid sequence	Competitive binding assay
Glycosylation and other PTMs analysis	TNFα blocker proliferation assay
Physicochemical Properties	TNFα blocker assay bioluminescent caspase 3/7 apoptosis assay
Aggregation analysis	Bioluminescent TNFα blocker reporter assay
High order structural analysis	*In vitro* biocomparability
Biosimilar Nonclinical *In Vivo* Package	**Biosimilar Preclinical/Clinical Laboratory Support Package**
Pharmacokinetic study	Bioanalysis and pharmacokinetic analysis
Toxicology study	Immunogenicity
	Immune system cell monitoring
	Neutralizing antibody assays
Formulation	**Lot Release and Stability Testing**
Preformulation	Pilot studies
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