BIOLOGICS TESTING SOLUTIONS

Stability Testing of Biopharmaceutical Products

Services

- Stability study design
- Advanced analytical methods

Protein, peptide, vector and plasmid products are particularly sensitive to environmental factors. At Charles River, we can perform stability studies to evaluate client biopharmaceutical products under various environmental conditions over a specific timeframe, recommend suitable storage and shipment conditions for drug substances and products, and determine the appropriate shelf life or retest period.

For more than 20 years, our team has helped clients develop and implement cGMP study plans that fulfill worldwide regulatory requirements. We provide a transparent, controlled and clearly documented course for every study we run, with thorough recordkeeping and reporting during and after study completion.

Stability Study Design

Our team bases all study designs on the International Conference on Harmonisation (ICH) guidelines *Q1A(R2): Stability Testing of New Drug Substances and Products and Q5C: Quality of Biotechnological Products – Stability Testing of Biotechnological/Biological Products*. Where possible, we apply bracketing and matrix designs in accordance with ICH document Q1D.

Shelf life is commonly estimated using results from both real-time stability and accelerated stability tests. In real-time stability testing, a product is stored at recommended storage conditions and monitored until it fails product specifications. In accelerated stability testing, a product is stored at elevated stress conditions (e.g., high temperatures and/or humidity). Degradation at the recommended storage conditions can then be predicted using known relationships between the acceleration factor and the degradation rate.

Charles River also supports forced degradation programs with studies that use extreme storage conditions in order to increase the rate of degradation. Due to the non-linear nature of protein degradation kinetics, these studies have limited value in shelf-life prediction for biopharmaceutical products. However, because they provide information on product breakdown and degradation pathways, forced degradation studies are particularly useful in early drug development to improve formulation and assist with the determination of storage conditions to control product stability.

EVERY STEP OF THE WAY

For biopharmaceutical products, long-term stability studies are conducted under the intended storage conditions, with shorter duration studies performed at higher temperatures to support in-use stability and shipping conditions. Lower temperature conditions are often included in the program to provide baseline non-stressed values and to prevent delays if the intended storage condition proves to be unsuitable.

Advanced Analytical Methods

Our team is skilled in a wide range of stability indicating analytical techniques using the latest instrumentation including:

- 1D and 2D SDS-PAGE
- Western blot
- Isoelectric focusing
- Peptide mapping of proteins and peptides using reverse-phase HPLC with UV and/or mass spectroscopy detection
- Stability-indicating chromatography (e.g., reverse-phase, size exclusion ion exchange and hydrophobic interaction chromatography)
- Sulfhydryl analysis
- N- and O-linked glycosylation/carbohydrate analysis
- Capillary electrophoresis including cIEF ,CE-SDS and CZE
- Protein content/concentration
- Spectrophotometric analysis (e.g., UV-Vis, fluorescence and circular dichroism)
- Determination of pH, dissolution, appearance and color
- Formulation-specific testing (e.g., subvisible particulates, moisture content)
- Total active ingredient determination by ELISA or immuno-ligand assay
- Potency assays including cell-based, in vivo models, ELISA and binding by SPR
- Container closure integrity
- Endotoxin, microbial enumeration and sterility testing