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Stability Testing of a Biopharmaceutical Protein

Protein and plasmid products are particularly sensitive to environmental factors. At Charles River, we can perform stability studies to evaluate your biopharmaceutical product 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.

In Vivo Stability Study Design

Real-time, *in vivo* stability studies are offered for clinical trial samples and for release testing to determine the potency of the product at predetermined timepoints over a 12-, 24- or 36-month period. Charles River offers regular communication and flexibility regarding your testing schedule to ensure that these critical stability timepoints are met.

Stability Study Design

Study designs are based 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, bracketing and matrixing designs in accordance with ICH document Q1D are applied.

The extent of a stability program depends upon the actual status of the product along the drug development process. Accelerated stability studies are designed to increase the rate of degradation of the drug by using extreme storage conditions. These types of studies are usually performed early in drug development for formulation improvement and shelf-life prediction. They have limited value in shelf-life prediction for biopharmaceutical products due to the non-linear nature of protein degradation kinetics; however, they do provide information on breakdown products that assist in the development of stability-indicating analytical methods.

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. Back-up, lower temperature conditions are often also included in the program to prevent delays if the intended storage condition proves to be unsuitable.

Analytical Methods

- 1D and 2D SDS-PAGE, reducing and non-reducing conditions
- Western blot
- Isoelectric focusing
- Peptide mapping and enzymatic mapping of proteins and peptides sing reversed-phase HPLC
- Chromatography, including reversed-phase, size exclusion and ion exchange
- Carbohydrate analysis
- Capillary electrophoresis
- Protein content assays
- Spectrophotometric analysis
- Determination of pH, appearance and color
- Sub-visible particulates, moisture content and other formulation-specific tests
- Total active ingredient determination by ELISA or immuno-ligand assay
- Potency assays
- Endotoxin, microbial enumeration and sterility testing

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Stability studies are conducted to support clinical trials, provide data for the product license application, support subsequent manufacturing changes and for post-marketing commitment purposes with bulk drug substances and finished products.

Sample Storage

Charles River utilizes fully qualified environmental chambers, walk-in rooms and freezers that fulfill all of the requirements established by the ICH guidelines. All facilities are continuously monitored through computerized systems with 24-hour contact to laboratory staff. A back-up plan is in place and sufficient back-up systems are available in the unlikely event of a long-term system failure. All chambers are validated and therefore compliant with current Good Manufacturing Practice (cGMP). They are also routinely inspected and revalidated.

Charles River offers extensive knowledge, experience and laboratory resources for your important stability testing.

- Studies are CGMP-compliant and fulfill worldwide regulatory requirements
- Clearly documented study plan developed
- Transparent and controlled records during and after study completion

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