Stability ICH

STABILITY SCIENCE FOR BETTER MEDICINES

Biologics Stability Testing

10 Critical Tests for Quality, Safety and Shelf-Life

Biologics stability testing evaluates how product quality changes over time and under stress.
It helps define shelf life, storage conditions, transport requirements and in-use handling.

10 Essential Stability Tests

Appearance & Visible Particles

Monitors changes in color, clarity and the presence of visible particles (e.g., turbidity, precipitate) that may indicate degradation.



Potency / Bioactivity

Confirms biological activity (e.g., binding, cell-based or functional assays) to ensure maintenance of the intended effect throughout shelf life.



Purity & Aggregates

Assesses product purity and levels of aggregates and higher-order species (e.g., by SEC, CE or MALS).



Charge Variants

Monitors changes in charge heterogeneity (e.g., by cation/anion exchange) that can arise from modification (e.g., deamidation, sialylation).



Identity / Intact Mass

Confirms molecular identity and monitors structural integrity (e.g., by LC-MS, intact mass or peptide mapping).



Subvisible Particles

Measures subvisible particles (e.g., 0.1–10 µm and ≥10 µm) to assess particle formation (e.g., by light obscuration or micro-flow imaging).



pH & Osmolality

Monitors pH and osmolality, which can affect protein stability, structure and aggregation risk.



Sterility / Microbial Control

Confirms absence of microbial contamination (e.g., sterility test, bioburden or endotoxin) to ensure product safety throughout the stability period.



Freeze–Thaw Stability

Evaluates the impact of repeated freezing and thawing on quality (e.g., aggregation, potency and particle formation) under realistic handling conditions.



In-Use / Reconstitution Stability

Assesses product stability after reconstituation or during in-use comdations (e.g., diluted drug, infusion holding time, or multi-dose use).



Common Degradation Risks

Aggregation

Formation of dimers or higher-order species that can reduce potency and increase immunogenicity.

Oxidation

Chemical modification (e.g., of Met, Trp or Cys) that can affect structure, activity and stability.

Deamidation

Conversion of Asn or Gln to acidic forms, which can change charge, structure and biological activity.

Fragmentation

Cleavage of the protein (e.g., at sensitive sites) that can lead to loss of activity or increased heterogeneity.

Adsorption / Particle Formation

Loss of product to surfaces (e.g., container or tubing) or formation of proteinaceous particles (e.g., glass, silicone or formulation effects).

What to Watch

- **Temperature excursions** — can accelerate degradation, aggregation and loss of potency.
- **Agitation** — may induce aggregation and particle formation (e.g., during shipping or handling).
- **Light** — can cause photochemical degradation (e.g., oxidation of sensitive residues).
- **Container-closure interactions** — potential adsorption, leachables or extractables that can affect stability.
- **Formulation drift** — changes in pH, osmolality or excipient levels that may impact stability.

Why Stability Testing Matters

Protects Product Quality

Ensures the biologic remains safe, potent and consistent over time.

Supports Shelf-Life Assignment

Provides the data needed to set a scientifically justified expiry date.

Strengthens Cold-Chain Decisions

Informs appropriate storage, shipping and handling conditions (e.g., 2–8 °C, frozen).

Reduces Patient Risk

Minimizes the chance of administering a degraded or suboptimal product.

Key Takeaway

Stability programs for biologics must combine orthogonal analytical methods and product-specific study design.

Reference framework: ICH Q5C, ICH Q1A(R2), ICH Q2(R2), WHO stability guidance.

