BioReliance
Analytical Services

Complete Stability Testing

At BioReliance, Analytical Services assists clients in evaluating the stability of their drug substance and drug product to ensure that it remains safe, stable, and effective in all conditions. Stability testing is used to demonstrate short and long term stability of a biologic after exposure to various environmental conditions such as temperature, humidity, light and container/closure interactions. Because of the sensitive composition of most biopharmaceuticals, evaluation of the stability of a drug substance and drug product is a necessary part of developing a licensed or registered product. Data from these stability studies is used to recommend storage conditions, re-test intervals, and shelf-life.

In order to establish a stability profile, specific assays are used to detect any changes in product identity, purity, and potency. A documented stability program with validated analytical assays should be used to detect these changes during storage. Stability studies should include an assessment of both drug substance and drug product to provide data that demonstrates that the product retains its efficacy throughout its shelf life. At BioReliance, we assist our clients in customizing stability protocols which are designed to meet their product specific needs and the requirements outlined by ICH **(Table 1)**.

Table 1: Complete Stability Assays

Full Stability Assays					
Assay Name	Recombinant Protein	Monoclonal Antibody	Method	Purified Bulk	Finished Product
Glycan Profiling	✓	✓	LC-MS, HPLC	✓	✓
Molecular Weight	✓	✓	LC-MS, SDS-PAGE	✓	✓
Antibody Subunit Analysis		✓	LC-MS	✓	
SEC	✓*	✓*	UHPLC	✓*	
RP	✓*	✓*	UHPLC	✓*	
IEX	✓*	✓*	UHPLC	✓*	
Charge Profile	✓	✓	CE, IEX, IEF	✓	✓
N-Terminal Sequencing	✓	✓	LC-MS		✓
SDS-PAGE/CE SDS	✓	✓	SDS-Page or cSDS		✓
Appearance and Description	✓	✓	Visual		✓
Moisture by Karl Fischer	✓	✓	KF		✓
Osmolarity (liquid)	✓†	✓†	Osmometer		✓†
pH (liquid)	✓†	✓†	pH		✓†

** HPLC method depends on sample specification. † indicates liquid sample.*

Note: Inclusion of assays is specific to client needs. All assays may not be needed or more assays may be recommended depending on client sample.

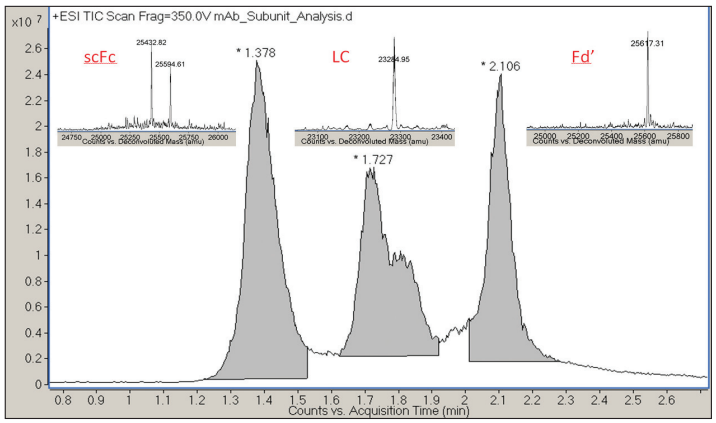

Figure 1: Subunit Analysis of mAb standard.

State-of-the-art instrumentation and cGMP capabilities provide results you can trust

Reliable service with fast turnaround delivers data on time

Analytical testing programs are designed by industry experienced scientists to suit your needs

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Analytical Services

Stability Protocol

A stability protocol is custom developed to prepare a stability indicating profile for the product. The stability protocol should contain information about the product to be tested, the sampling process, the duration of the study, the number of samples required, the storage conditions and the methods of analysis. We work with our clients to develop stability protocols that comply with ICH guidelines and are customized for their drug substance or product (Table 2).

Storage Conditions

Biologics require precise storage conditions because of the sensitivity of these products to environmental conditions. Thus, drug substances and drug products should be studied in storage conditions that evaluate their sensitivity to temperature, humidity, light exposure and product container/closure reactions. The conditions and length of studies should cover storage, shipment, and subsequent use[1]. BioReliance offers a full range of stability storage conditions, including conditions for accelerated as well as forced degradation studies.

Table 2: Example stability testing protocol

Timepoint (months)	Short Term Storage	Long Term Storage
0	A-E	A-E
1	A-E	A-E
2	A-E	A-E
3	A-E	A-E
6	A-E	A-E
9	A-E	A-E
12	A-F	A-F
18		A-E
24		A-F
36		A-F

A = Appearance, pH, protein concentration, particulate testing
B = Electrophoretic Analysis
C = HPLC analysis
D = Peptide Mapping
E = Functional Assay, such as ELISA or bioassay
F = Bioburden, sterility, potency testing

Testing Frequency

The ICH guideline recommends that the frequency of testing at long term storage conditions for a product with a shelf life of at least 12 months should be every 3 months for the first year, every 6 months for the second year, and annually thereafter for the duration of the shelf life[1]. The testing frequency for accelerated storage conditions is a minimum of three time points for a 6 month study.

References:

1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), Quality Guidelines, Q1A(R2) Stability Testing of New Drug Substances and Products

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