



Stability studies at different stages

- 1) Stress- and accelerated Testing with drug substances
- 2) Stability on pre-formulation batches
- 3) Stress testing on scale-up Batches
- 4) Accelerated and long term testing for registration
- 5) On-going Stability testing
- 6) Follow-up Stabilities

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Stability tests according ICH

- “Stability Testing of **New Drug Substances** and Products” .
- “Quality of **Biotechnological** Products: Stability Testing of Biotechnology/ Biological Drug Products”
- “**Photostability Testing** of New Drug Substances and Products”
- “Stability Testing of **New Dosage Forms**”

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Table 9.1 ICH storage conditions for general, refrigerated and frozen drug substances and products (ICH Guideline Q1A).

Study	Storage condition	Minimum data required before regulatory submission
General		
Long-term	25 ± 2 °C and 60 ± 5% RH	12 months
	30 ± 2 °C and 65 ± 5% RH	
Intermediate Accelerated	30 ± 2 °C and 65 ± 5% RH	6 months
	40 ± 2 °C and 75 ± 5% RH	
Refrigerated		
Long-term	5 ± 3 °C	12 months
Accelerated	25 ± 2 °C and 60 ± 5% RH	6 months
Frozen		
Long-term	-20 ± 5 °C	12 months

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Table 9.2 ICH climatic zones and their associated long-term storage conditions.

Climatic zone	Definition	Long-term storage conditions
I	Temperate	21 °C, 45% RH
II	Subtropical and Mediterranean	25 °C, 60% RH
III	Hot and dry	30 °C, 35% RH
IVA	Hot and humid	30 °C, 65% RH
IVB	Hot and very humid	30 °C, 75% RH

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Table 49.3 Examples of recommended minimum stability testing schedules for pharmaceutical products

Storage time (months)	Products intended to be stored in a refrigerator		Product intended to be stored in ambient conditions	
	Long-term 5 °C	Accelerated Zone II 25 °C/60% RH Zone IVA 30 °C/65% RH Zone IVB 30 °C/75% RH	Long-term Zone II 25 °C/60% RH Zone IVA 30 °C/65% RH Zone IVB 30 °C/75% RH	Accelerated 40 °C/75% RH
0	√	√	√	√
3	√	√	√	√
6	√	√	√	√
9	√		√	
12	√		√	
18			√	
24			√	
36			√	

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Testing scope for Solid dosage

Tablet & Capsule

- **Physical-chemical properties**
 - Appearance
 - Elasticity
 - Mean mass
 - Moisture
 - Hardness
 - Disintegration
 - Dissolution
- **Chemical properties**
 - Assay
 - Degradation
- **Microbial properties**
- **Container closure system properties**
 - Functionality tests (e.g. extraction from blister)

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Testing scope for Oral liquid form

- **Physical-chemical properties**
 - pH
 - Color & clarity of solution
 - Viscosity
 - Particle size distribution (for oral suspensions only)
- **Microbial properties**
- **Chemical properties**
 - Assay
 - Degradation products
 - Degradation preservatives
 - Content antioxidants
- **Container closure system properties**
 - Functionality tests

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Testing scope for *LIQUID FORMS* inj. and *PARENTRAL*

- **Physical-chemical properties**
 - pH
 - Loss on weight
 - Color & clarity of solution
- **Container closure system properties**
 - Functionality tests
- **Chemical properties**
 - Assay
 - Degradation products
 - Degradation preservatives
 - Content antioxidants
- **Microbial properties**

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Testing scope for *SEMI LIQUID FORMS*

- **Physical-chemical properties**
 - Appearance, odor, homogeneity, consistency
 - Loss on weight, Viscosity
 - Content uniformity (within the container)
- **Chemical properties**
 - Assay
 - Degradation products & preservatives
 - Content preservatives
 - Degradation
 - Content antioxidants
- **Container closure system properties**
 - Functionality tests
- **Microbial properties**

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Suggested analytical methods for various dosage forms, depending upon the active drug:

DOSAGE FORM	ANALYTICAL METHOD													
	WT	VOL	PH	OSM	RI	SP	GR	MP	UV/VIS	HPLC	GC	IR	STERIL	ENDO
Bulk substances	—	—	*	—	*	—	*	*	*	*	*	*	—	—
Powders	*	—	—	—	—	—	—	—	—	*	*	—	—	—
Capsules	*	—	—	—	—	—	—	—	—	*	*	—	—	—
Tablets	*	—	—	—	—	—	—	—	—	*	*	—	—	—
Lozenges	*	—	—	—	—	—	—	—	—	*	*	—	—	—
Suppositories	*	—	—	—	—	*	*	—	—	*	*	—	—	—
Sticks	*	—	—	—	—	*	*	—	—	*	*	—	—	—
Solutions	*	*	*	*	*	*	—	*	*	*	*	—	—	—
Suspensions	*	*	*	—	—	*	—	—	—	*	*	—	—	—
Emulsions	*	*	*	—	—	*	—	—	—	*	*	—	—	—
Semisolids	*	—	—	—	—	*	*	—	—	*	*	—	—	—
Gels	*	*	*	—	*	*	—	—	—	*	*	—	—	—
Ophthalmics, Otics, and Nasals	*	*	*	*	*	*	—	*	*	*	*	—	*(Ophthalmic only)	—
Inhalations	*	*	*	*	*	—	—	*	*	*	*	—	*	—
Injections	*	*	*	*	*	*	—	*	*	*	*	—	*	*