

**Table 7** Stability Testing on the Critical Path

Step of development	Stability information	Needed for	Time to availability from start
1	Preliminary stability profile of drug substance	Start of predevelopment	6 weeks
	Stability profile of drug substance	Base for minimum shelf life phase I	16 weeks
3	Minimum shelf life toxicological samples	Release of toxicological samples	8 weeks
	Minimum shelf life clinical samples phase I	Release of clinical trial batch phase I	9, 15 weeks
	Minimum shelf life clinical samples phase II	Release of clinical trial batch phase II	15, 27 weeks
	Minimum shelf life clinical samples phase III	Release of clinical trial batch phase III	15, 27 weeks
4	Stability report for registration application	Filing data for registration application	(Release of 3d batch for accelerated and long-term testing) 15 months

The drug substance to be investigated should have been selected as the most suitable salt form.

## 2.2. Application of the Basic Principles

Selection of batches and samples: experimental batch; it must comply with the acceptance limits of the preliminary testing specification, as far as they are available. The impurity profile, particle size distribution, and the surface area are especially important.

Test criteria: appearance, physical properties, assay, decomposition.

Analytical procedure:

Specific for stability testing

Orientalional validation at the beginning specificity, linearity, quantitation limit  $\geq 0.05\%$  of the drug substance.

Preliminary validation at the end in addition: accuracy, range, repeatability, robustness for drug substance and decomposition products

Specifications: at the end: preliminary release specifications.

Storage conditions:

In open containers: 25°C/60%, 25°C/75%, 30°C/70%, 40°C/75%.

In standard packaging material: 40°C, 50°C, 60°C, 70°C.

Storage period: Until equilibrium is reached at open storage, < 3 months.

Testing frequency:  $\leq 4$ .

Number of batches per investigation: 1.