As phases I through III progress, experience with analytical procedures and shelf life specifications increases. The results and stability information derived from them become steadily more reliable.

Finally, the stability program is designed in such a way that stability predictions are verified by the results of long-term tests.

There is thus still the possibility of replacing batches if necessary.

Like the overall system of stability testing, the stability program for clinical samples is systematically structured in such a way that the aggregate available information is continuously augmented (Table 11).

Table 11 Number of Dosages and Packaging Materials

Stage of development	Tests[a]	Number of dosages	Number of packaging materials	Total number	Derived information
Drug substance	Stress and acceleration tests	1	1	1	Retest date ≥2 years
Clinical phase I	40°C/1.5 months	≥2	2	≥4	3 months
	40°C/3 months	≥2	2	≥4	6 months
Clinical phase II	60°C/3 months	2[b]	2	4	12–18 months
Clinical phase III	70°C/3 months	1[b]	3	3	24–36 months
				≥16	

[a] A confirmatory long-term test is conducted concurrently with stress and acceleration tests.

[b] If more than 2 dosages are used in clinical phase II, ≥2 applies; if more than 1 dosage is used in clinical phase III, ≥2 also applies. This data in the table are therefore minimum limits.

2.13. Extension of the Derived Minimum Shelf Life

A minimum shelf life is determined for clinical trial samples and can be extended as necessary if the corresponding tests yield favorable results. Parallel to the stress and accelerated tests, samples are stored at 25°C/60% r.h. in order to confirm and support the predicted minimum shelf life.

If all the predicted data and the data confirmed in long-term tests are within the minimum shelf life limits, they can be extended if necessary. For this purpose, a new prediction is performed and samples are stored at 25°C/60% r.h. to confirm the new minimum shelf life (see Table 12).

3. PERFORMANCE

The performance of the stress and confirmation studies in phases I–III is described.

The base forms the Stability Profile of the NME, the corresponding drug substance.