

ACCELERATED DEGRADATION STUDIES

Overview

Degradation at the selected temperature of storage often is too slow for real-time studies to be practical before determining whether a material can be used as a reference material, although real-time studies can continue in parallel with the initial use of the materials (35).

In principle, material is stored at a range of elevated temperatures and also at some reference temperature at which degradation is assumed to be insignificant. The activity of these samples is determined at known time intervals relative to the activity of the reference material stored for the same duration. It is important to always include a sample from the reference temperature at every testing and sufficient material should be placed in storage for this purpose.

The reference temperature should be less than the intended temperature of storage. These studies yield no direct information on the stability of the material at the reference temperature, although some indirect information can be obtained from the magnitude of the assay response of the reference material over time.

Typical Testing Protocol

At first, samples from the higher temperature storage sites (e.g., 56°C) are removed periodically and tested against samples from the reference storage temperature until significant degradation (20–30%) is observed. It is important not to use samples from the lower temperature storage sites early in the study. Such samples probably would show no significant degradation and would waste irreplaceable material (Table 5).

Attention is then focused on the next highest temperature storage sites (e.g., 45°C and 37°C). These are removed periodically and tested until significant degradation (15–25%) is observed. The study proceeds for a suitable period until degradation (5–10%) is observed at the lower storage temperatures (e.g., 20°C and 4°C). Subsequently, samples are assayed from all the available storage temperatures against samples from the reference storage temperature.

The frequency of testing will depend on the rate of degradation observed at the higher storage temperatures. Initially, in the absence of any prior knowledge of the degradation rate, a suggested protocol is one month, two months, three months, six months, and one year. On removal from storage

TABLE 5 Typical Testing Protocol for an Accelerated Thermal Degradation Study

Samples removed from storage site at time	Sample removed from given storage temperature					
	Reference temperature	4°C	20°C	37°C	45°C	56°C
1 mo	↓			↓	↓	↓
2 mo	↓			↓	↓	↓
3 mo	↓		↓	↓	↓	(↓)
6 mo	↓		↓	↓	(↓)	
12 mo	↓	↓	↓	↓		
Subsequent times	↓	↓	↓	↓		

Source: From Ref. 35.