daylight tubes, xenon lamps, tungsten–mercury lamps, laboratory light, and natural light. Instruments from Thermometric (4) are useful in measuring solid-state stability. Up to four independent calorimeter units can be used simultaneously with thermal activity monitor (TAM) III. A unit can be a 4-mL nanocalorimeter for measurements that require very high sensitivity, a 20-mL standard microcalorimeter, a multicalorimeter consisting of six minicalorimeters, or the semi-adiabatic solution calorimeter. The multicalorimeter increases sample throughput considerably and is used for applications where microwatt, rather than nanowatt, sensitivity is sufficient. TAM III also exists in a 48-channel version for screening applications or, in general, when high sample throughput is required. TAM III can be operated in isothermal, step-isothermal, or temperature scanning mode. The isothermal mode is the classical mode for microcalorimetric experiments. In the isothermal mode, the liquid thermostat is maintained at a constant temperature (±50 μK). Any heat generated or absorbed by the sample as a consequence of any chemical or physical process is measured continuously as a function of time. Step-isothermal mode is used to perform isothermal experiments at a number of temperatures in one single experiment. This is of particular interest for extracting temperature-dependent kinetic behavior for different kinds of processes. In the scanning mode, the temperature is scanned linearly over a certain interval. As the scanning rate is very slow, the sample can be considered to be in virtual thermal, chemical, and physical equilibria during measurement. For sample handling, a variety of ampoules and microreaction systems can be inserted in the calorimetric units, the type of which is determined by the experimental application.

The terahertz pulsed imaging (TPI)™ spectra 1000 system exploits the spectroscopic information within each TPI™ waveform to determine the chemical composition and the structural features of a sample (5) by using terahertz technology. Terahertz data are complementary to Raman spectroscopy. It also provides information on both high-frequency (just below IR) and low-frequency vibrational modes; the latter are difficult to assess in Raman spectroscopy, owing to the proximity to the visible excitation line. Terahertz spectral interpretation and instrumentation are similar to basic IR and are therefore easy to understand. The sample preparation techniques are the same as those used in IR and Raman spectroscopy. The unique spectral imaging characteristics of combining TPI and terahertz pulsed spectroscopy (TPS) can be used to investigate the applications of proteomics in the pharmaceutical industry. The TPI™ spectra 1000 can assist pharmaceutical companies in the rapid characterization of the stability and polymorphic forms of drugs. Many drug molecules after purification can crystallize in many different forms. These are known as polymorphs. Terahertz technology provides a rapid technique to identify different polymorphs.

In terms of the kinetics, light degradation in dilute solution is of first order; however, in more concentrated solutions, decomposition approaches pseudo-zero order. The reason for this is that as the solution becomes more concentrated, degradation becomes limited owing to the limited number of incident quanta and quenching reactions between the molecules. It should be noted that ionizable compounds, for example, ciprofloxacin, can show large differences in photostability between the ionized and unionized forms.

8.2.5 Regulatory Consideration in Stability Testing

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of