are needed. Methods such as XRD, DSC, FT-Raman spectroscopy, and microcalorimetry are currently the most widely used to evaluate crystallinity.

Near-infrared (NIR) spectroscopy is becoming an important technique for pharmaceutical analysis. This spectroscopy is simple and easy because no sample preparation is required, and samples are not destroyed. In the pharmaceutical industry, NIR spectroscopy has been used to determine several pharmaceutical properties, and a growing literature exists in this area. A variety of chemoinfometric and statistical techniques have been used to extract pharmaceutical information from raw spectroscopic data. Calibration models generated by multiple linear regression (MLR) analysis, principal component analysis, and partial least squares regression analysis have been used to evaluate various parameters.

### 3.5.5 X-Ray Diffraction

The determination of the average morphology is often a "bottleneck" in elucidating other important behaviors of large quantities of crystalline powders used in pharmaceutical development and processing.

X-rays are electromagnetic radiation of wavelength about 1 Å ($10^{-10}$ m), which is about the same size as an atom. They occur in that portion of the electromagnetic spectrum between gamma rays and the ultraviolet rays. The discovery of X-rays in 1895 enabled scientists to probe crystalline structure at the atomic level. X-ray diffraction has been in use in two main areas: for the fingerprint characterization of crystalline materials and for the determination of their structure. Each crystalline solid has its unique characteristic X-ray powder pattern, which may be used as a "fingerprint" for its identification. Once the material has been identified, X-ray crystallography may be used to determine its structure, that is, how the atoms pack together in the crystalline state and what are the interatomic distance and angle. X-ray diffraction is one of the most important characterization tools used in solid-state chemistry and materials science. The size and the shape of the unit cell for any compound can be most easily determined by using the diffraction of X-rays.

It is possible to use XRD techniques to estimate the average shape and "habit" of organic crystalline material using a single crystal. The relative intensities of the peaks in an XRD pattern from a sample exhibiting a "standard" preferred orientation correlate with the shape of the crystallites present. Models have been developed to yield a quantitative "enhancement" factor for each face. The combined simple forms morphology (CSM) of the material can be produced by indexing the observed faces and modifying the simulated Bravais–Friedel–Donnay–Harker (BFDH) morphology (7). The average shape of crystallites can be estimated from the CSM by multiplying each face by its enhancement factor.

### 3.5.6 Stability Testing

The regulatory authorities clearly define the protocols for the testing of drug products for stability during the shelf life. However, testing of drug substances at the preformulation level for stability evaluation offers several advantages and opportunities once the drug substances enter the formulation stage. First, it provides a clear idea about which types of dosage forms can be used. A highly unstable protein drug cannot be placed in anything but a highly preserved and protected parenteral form, as an example. The development of stability testing protocols starts with the development