of stability-indicating methods, the details of which can be readily found in any pharmaceutical analysis text or through the website of the U.S. FDA. The Q1A R2 (Stability Testing of New Drug Substances and Products) is a good starting place (8). Similar guidelines are provided for biotechnology and botanical products.

3.5.6.1 Moisture Isotherm

The crystalline structure can significantly affect a compound's tendency to absorb moisture, which can impact sample handling for analytical testing, formulation, stability, and product shelf life in the areas of varying humidity. For example, if a compound attracts water as it is exposed to rising humidity levels, each kilogram of material will contain more water and less of the compound as the humidity level increases. This could carry over to the formulation, where, as a consequence of the higher moisture content in the API, a subpotent formulation could be manufactured. Hence, drug manufacturers need this information in order to adequately control humidity and ensure uniform moisture to compound ratios across batches. They also need the information to design specific formulations and packaging that will maintain the stability of a finished product when it is shipped and stored in different environments. A compound may remain stable in the controlled humidity and temperature of a lab or manufacturing facility but may degrade if it acquires water when trucked across country or stored on a pharmacy shelf. For example, compound A may exist in two salt forms—a nonhygroscopic monohydrochloride form and a hygroscopic dihydrochloride form. The client needs to use the dihydrochloride form for a solid oral dosage. Increasing moisture levels in the formulation leads to localized areas of high concentrations of hydrochloric acid in the vicinity of the API molecules. The decision must then be made whether to develop a capsule formulation or a tablet formulation, as each has its own unique set of manufacturing and packaging challenges. While the basic generation of a capsule formulation may be the quickest route, initially, the need for extensive coating and or packaging may slow the entire process. These measures would be required to protect the product from moisture, as the generation of hydrochloric acid in the formulation could result in partial digestion of the capsule shell. For a tablet formulation, the application of a moisture impermeable coating may be a simpler process, and more options may be available to package the material in a protective environment. Knowing this information at the beginning of the process may save the client a considerable time, while providing some early direct on to the development of an appropriate and successful formulation. Experimental data can generate a lot of information regarding the characteristic behavior of the molecule. In addition to understanding the hygroscopicity of the compound, drug manufacturers should know whether their compound's vapor sorption is "reproducible" as humidity levels go up and down. One of our most useful instruments is the vapor sorption analyzer, which, among other things, subjects samples to increases and decreases in relative humidity (RH).

These studies involve weighing out a small sample and exposing it to a very dry atmosphere at low or high temperatures. Once the sample dries to a prespecified level, the humidity is raised in increments, for example, from 5% to 95%, while keeping the temperature constant. By weighing the sample at each increment, one can determine how much moisture the compound acquires at a given percentage of RH. This is very important information for predicting the stability and shelf life. We can then determine whether vapor desorption is reproducible by weighing the sample as we decrease the