

the API's stability requirements. Obviously the intended application of a stability-indicating method is for monitoring the stability of a given drug in a finished product and would require assessment of the method's stability-indicating properties. One specialty application of a stability-indicating method is cleaning validation testing, which would require assessment of its stability-indicating properties, as holding time (of the swaps) would be a critical factor. Other applications such as product release, performance testing (i.e., dissolution testing) and in-process testing do not require this assessment. Some pharmaceutical houses still (but now less commonly due to technological advances and overall industry practice) utilize a non-stability-indicating method such as UV, for product release, and an HPLC method for stability testing. However, whenever there is a hold time issue, common in dissolution or in-process testing, it would be prudent to assess the method for its stability-indicating properties before its intended application.

Other chromatographic separation methods, such as chiral chromatography (CC), thin-layer chromatography (TLC), gas chromatography (GC), and (increasingly) capillary electrophoresis (CE), are stability-indicating and stability-specific methods. Still the most prevalent technique is reversed-phase HPLC alone or coupled with ion-suppression, which accounts for 85% or more of the general pharmaceutical applications.

Nonchromatographic and spectroscopic techniques such as titrimetry, atomic absorption, UV spectrophotometry, and infrared spectroscopy, while precise, are not considered stability-indicating, and as such not suitable for stability assessment applications.

### 3. OVERVIEW OF THE METHOD DEVELOPMENT PROCESS

Before beginning with actual experimentation it would be advantageous to view method development from a broader perspective. The method development process can be visualized from a high-level process map perspective better to define the general steps encountered to achieving the end product, a stability-indicating method.

