What level of accuracy and precision would be needed?
The method is designed for what type of matrix? How many types of sample matrices are encountered?
Is the method developed using certain equipment transferable to the control laboratory, which may not have the same equipment?
Will the method be used for a few samples or many samples?
What chromatographic parameters are needed?
How much resolution is needed?
What is a suitable/acceptable separation time?
What is a suitable column pressure?
How much sensitivity is required?
Is an internal standard needed?
Are there any detection issues? Most analytes absorb in the UV region of the spectrum.
Does integration use peak area or height?
Is the mode isocratic or gradient?

6. SELECTION OF THE CHROMATOGRAPHIC MODE

6.1. The Different Modes of Liquid Chromatographic Methods (HPLC)

While there are a number of HPLC methods available to the development chemist, perhaps the most commonly applied method is reversed-phase. Reversed-phase and reversed-phase coupled with ion-pairing probably account for more than 85% of the applications for a typical pharmaceutical compound. The typical pharmaceutical compound is considered to be an API of less than 1,000 daltons, either soluble in water or in an organic solvent. The water-soluble API is further differentiated as ionic or nonionic which can be separated by reversed-phase. Similarly, the organic soluble API can be classed as polar and nonpolar and equally separated by reversed-phase. In some cases, the non-polar API may have to be separated using adsorption or normal phase HPLC, in which case the mobile phase would be a nonpolar organic solvent. For those "special" compounds that do not fall into this category (API>1000 daltons [biopharmaceuticals], isomers or enantiomers), other chromatographic modes may be necessary for separation. These include ion-exchange and chiral chromatography. In this discussion of developing a stability-indicating HPLC method, only reversed-phase will be discussed.

6.2. Reversed-Phase Chromatography

Thus given the limited number of methods with stability-indicating properties, it is probable that the method selected would be HPLC. Two very advantageous characteristics of HPLC, its discriminating power and its ability to operate at room temperature or at low elevated temperature, would not contribute to the degradation of the analyte. It is further assumed that the API is of low molecular weight (<1000 daltons), organic in nature (versus inorganic), and not a biopharmaceutical. These restrictions apply to a large percentage of the pharmaceuticals and enable them to be readily separated using reversed-phase HPLC, and sometimes with the aid of an ion-suppression agent, in roughly 85%