Stability is not synonymous with chemical kinetics, yet most of the rate-limiting phenomena are either associated with chemical reactions or are describable by some equation system that bears a resemblance to those encountered in chemical kinetics. It is, therefore, of importance to lay the proper kinetic foundation before discussing the actual phenomena encountered in dosage forms.

These fundamental principles are most conveniently described by solution kinetics. The simpler a system is, the easier it is to make it reproducible, and it is therefore not surprising that the largest number of pharmaceutical publications on the subject of kinetics deal with solution systems. Furthermore, the more dilute a system is, the more it will adhere to ideal laws, and hence the largest number of publications to be found deal with dilute systems. There are obviously pharmaceutical dosage forms that are solutions, viz. oral, parenteral, nasal, ophthalmic, and otic solutions. Of these, it is only the parenteral and ophthalmic solutions that are chemically fairly simple, i.e. contain only a few number of components. These are systems that would behave similarly to the patterns described in, for instance, the chemical literature. In oral solutions, there are many ingredients (sweeteners, solubilizers, etc.), so that, here, one would expect definite vehicle effects and interaction possibilities.

The Stability Guidelines make certain requirements on basic stability that are best elucidated (or only elucidated) through solution kinetics: First of all it is necessary to develop a stability-indicating assay. This is defined in lines 111 of the 1987 Guidelines as "Quantitative analytical methods that are based on the characteristic structural, chemical, or biological properties of each active ingredient of a drug product and that will distinguish each active ingredient from its degradation products so that the active ingredient content can be accurately measured." The 1993 ICH Guidelines state,

> Analytical test procedures should be fully validated and the assays should be stability-indicating. The need or the extent of replication will depend on the results of validation studies (194–196).
>
> The focus may instead be on assuring the specificity of the assay ... of identified degradants as indicators of the extent of degradation via particular mechanisms (386–389).

This means that the assay must be capable of detecting quantitatively the amount of parent drug present, and identify, and to some degree quantitate, the decomposition products. Lines 265–277 of the 1987 Guidelines state, "When degradation products are detected, the following information about them should be submitted when available:

(a) Identity and chemical structure,
(b) cross-reference to any available information about biological effect and significance at the concentrations likely to be encountered,
(c) procedure for isolation and purification,
(d) mechanism of formation, including order of reaction...,
(e) physical and chemical properties,
(f) specifications and directions for testing for their presence at the levels or concentrations expected to be present."

Lines 141–144 further state that "the stability-indicating methodology should be