II. DETERMINATION OF COMPONENT RANGES

The first step in the optimization of a topical drug delivery system is selecting a preliminary formulation and determining the component ranges to be optimized by conducting phase behavior studies. Because these studies require preparation of a large number of samples, laboratory robotic techniques can be used to automate the quantitative dispensing and mixing of the components. Although the data that result from evaluating each of the samples can be represented by various techniques, plotting the data to compose a binary or ternary phase diagram is the method used in this chapter. Representing the data with binary or ternary diagrams is the most efficient way of presenting all of the equilibria for systems containing only pure components. For complex systems typical of industrial applications, binary and ternary diagrams provide a method of mapping (characterizing) the "phases" whose component composition range must be known. Thus, the general usefulness of binary and ternary phase diagrams warrants the following detailed description of how to assimilate the information provided by these diagrams. This tutorial on phase diagrams will be followed by a general, yet detailed description of the laboratory robotic techniques that are useful in preparing the samples required to complete the phase diagrams. Remember, adequate characterization of any disperse system is required to guarantee smoothness and continuity throughout the composition range to be optimized.

A. Phase Behavior

Disperse systems are unique among pharmaceutical dosage forms because the physicochemical interactions between the components dominate the stability of the system. Small changes in the component composition can completely destabilize or dramatically improve the stability of the dispersion. A well-characterized example would be the stable emulsion region for the water–*p*-xylene–decaoxyethylene glycol nonyphenol ether system. In this system the stability of the emulsion dramatically increased when the surfactant concentration was changed from 3 to 4 wt% (4). This dramatic change in physical stability was related to the formation of lamellar liquid crystalline bilayers around the oil droplets. The formation of a third phase (e.g., a liquid crystalline phase) is now a common method of increasing emulsion stability (5). Other examples of small compositional changes affecting product properties would include the effect of pH on clay suspensions or the effect of solids content on the melting point of a suppository.

To understand dispersion stability, it must be realized that changes in stability are the result of changes in the phase behavior