hydrolysis of lipids and lecithins, resulting in liberation of free fatty acids, which lowers the pH of the emulsions. To counter the pH dropping during autoclaving, it is suggested to adjust the pH of the emulsion to slightly alkaline pH (8.0) before autoclaving (Floyd, 1999). If the components of a particular drug-emulsion formulation preclude autoclaving owing to stability problems, sterile filtration of the product may be a viable alternative, requiring that the emulsion droplets pass through a 0.22 μm pore (Lidgate et al., 1992). There are also some reports of emulsions being successfully lyophilized; for example, an HIV protease inhibitor, AG1284, was solubilized in an Imwitor® 742/Tween 80/Span 80 emulsion, which could be lyophilized and reconstituted without loss of viability and potency (Chiang et al., 1995).

## CHARACTERISTICS OF EMULSIONS

There are a number of physicochemical properties of emulsions that are important to consider when developing an emulsion formulation for a drug. These include, but are not limited to, particle (droplet) size, viscosity, osmolarity, and zeta potential, which are used to monitor the physical stability of emulsions. Assays of potency and degradant levels are used to monitor the chemical stability of emulsions.

*Particle (droplet) size.* An important parameter is the particle (droplet) size of the emulsion. A variety of instruments and techniques exist for monitoring particle size. The most widely used techniques rely on laser light scattering, as reviewed by Tadros et al. (2004). Instrument manufacturers include Nicomp, Coulter, Horiba, Sympatec, and Malvern. Electron microscopy has also been used, but artifacts introduced by fixing techniques should be carefully controlled. Typically, emulsions produced by the methods described earlier yield particle sizes of 100–1000 nm; particle sizes less than 200 nm are generally required for emulsions used intravenously.

*Viscosity.* This parameter can be monitored by standard rheological techniques. The rheological properties of emulsions, reviewed by Sherman (1983), can be complex, and depend on the identity of surfactants and oils used, ratio of disperse and continuous phase, particle size, and other factors. Flocculation will generally increase viscosity; thus, monitoring viscosity on storage will be important for assessing shelf life.

*Osmolarity.* Osmolarity of a conventional emulsion is largely determined by components of the continuous phase, and the disperse phase may contribute little to the osmolarity. Thus, water-soluble excipients such as glycerol are frequently added to adjust tonicity of emulsions intended for parenteral use. Conventional techniques can be used for monitoring osmolarity. Owing to possible changes in emulsion structure on freezing, instruments that rely on vapor pressure lowering are more suitable for monitoring osmolarity of emulsions than those based on freezing point depression.

*Zeta potential*. Zeta or electrokinetic potential is related to the surface charge of the emulsion droplets and it is generally measured by electrophoretic techniques. The zeta potential is highly dependent on the surfactants used. Yamaguchi et al. (1995) compared the properties of otherwise identical 10% soybean oil emulsions prepared from two different sources of lecithin: one containing 99% PC and the other containing only 70% PC, with phosphatidyl ethanolamine (PE) comprising much of the remaining phospholipid. At pH 4, 5, 6, and 8, the purified (99%) lecithin emulsion had zeta potentials of 5, −3, −8, and −30 mV, respectively, reflecting the zwitterionic nature of PC. In contrast, the crude (70%) preparation had zeta potentials of −15, −30, −45, and −60 mV, respectively, at the same pH values, reflecting the ionization properties of the free amino group of the PE (Yamaguchi et al., 1995). A charged drug molecule at the interface will also affect the zeta potential.

*Chemical stability.* Certain emulsion components, especially those derived from unsaturated lipids, can give rise to undesirable degradation products on storage. These can include