

It is obvious that the small globule count does not change much, but that the intermediate count changes a lot. (The large globule count would then change in complement fashion to the intermediate count, and this was confirmed by the microscopy results.) What is important in this particular case (the system tested was a parenteral fat emulsion) is that there was formation of large oil droplets (not visible to the naked eye), and that these could have had a bearing on the toxicity of the product. This demonstrates that one method in itself is not enough, and that not one but several methods should be considered.

Reng (1984) has advocated electrical conductivity as an overall, common means of determining the state of dispersion of an emulsion system, and he shows that this parameter changes significantly over short periods of time, if the emulsion system is not satisfactory.

### 4.3. Stability of the Emulsifier/Protective Colloid System

The other phenomenon that may happen, which affects droplet size, is chemical breakdown in the surfactant. Nonionic surfactants are frequently used, and they are esters that may hydrolyze or interact with other components of the emulsion. Part of the formulator's job is, in independent experiments, to determine the pH profile and interaction potential of the surfactant (in a system simply consisting of the aqueous phase) with the other additives of the emulsion system. This can be done simply by cloud times (at accelerated temperatures) if the acid or alcohol from the hydrolysis or the interaction product is poorly soluble (as it is in the case of polysorbates and arlacels).

The problem with nonionic surfactant hydrolysis is exactly that it produces a fatty acid, which may become part of the oil phase and hence (aside from providing less coverage of the oil droplet) change the emulsion characteristics of the system.

In general the formulator also determines the HLB (hydrophilic/lyophilic balance) of the system he works with and matches it to the surfactant used [Atlas Chemical Company (now ICI Americas), 1963]. The HLB of the emulsifier can be adjusted by mixing two emulsifiers, e.g., arlancel 85 has an HLB value of 2.0 and polysorbate 80 one of 16.5. If an emulsion system required an HLB of 10 for instance, then the ratio of polysorbate ( $x$ ) to arlancel ( $1 - x$ ) would be given by

$$2(1 - x) + 16.5x = 10 \quad (10.19)$$

or

$$x = \frac{8}{14.5} = 0.55 \quad (10.20)$$

### 4.4. Emulsion Type

In emulsion formulation, the type of emulsion is of concern. If it is desired to make an oil-in-water emulsion (o/w, i.e., oil is the discontinuous phase), then it is important that phase inversion not occur. Investigating this possibility must be a task in the stability program (and is usually carried out by the formulator, not the preformulator). Most often phase inversion is associated with creaming and separ-