With regard to the interaction of solubilization, dispersion, digestion, and absorption, Porter et al. (2008) have outlined seven guidelines for design of lipid-based formulations:

1. It is critical to maintain drug solubility in the formulation after dispersion, and after digestion.
2. Properties of the colloidal species formed after digestive processing are probably more important than properties of the formulation itself in enhancing absorption. Higher proportions of lipid (>60%) and lower proportions of surfactant (<30%) and cosolvent (<10%) generally lead to more robust drug solubilization after dilution and digestion.
3. While MCT may afford greater drug solubility and stability in the formulation, LCT facilitate more efficient formation of bile salt-lipid colloidal species and therefore may yield higher bioavailability.
4. Type IIIB SMEDDS formulations give lower droplet sizes after dispersion. However, they are more dependent on the surfactant properties employed; non-digestible surfactants generally give higher bioavailability.
5. Dispersion of Type IV formulations containing two surfactants with cosolvent is likely to be more efficient than those with a single surfactant.
6. Type IV formulations may give higher drug solubility, but must be designed carefully to avoid drug precipitation after dispersion.

## FINAL DOSAGE FORMS OF LIPID-BASED DRUG DELIVERY SYSTEMS

Lipid-based formulations can be (1) ready-to-use emulsions, (2) liquid systems that are either diluted with water or juice before administration, or (3) presented as liquid-filled capsules (Table 11.3). While capsules generally represent the most convenient dosage form, liquids are more acceptable to pediatric and geriatric patient populations. Furthermore, at early stages of drug development, liquid lipid-based formulations provide a relatively rapid means of entering First-in-Human studies due to the ease of manufacture of the formulation. The purpose of First-in-Human studies is generally for proof-of-concept of the drug's safety and efficacy, and the primary goal is usually to reach the clinic as fast as possible. In these studies, for greater patient or volunteer acceptance, it is desirable to dilute the formulation in juice, water, or other aqueous vehicle immediately before dosing; the administration of the resulting emulsion can also lead to more uniform dosing and absorption. If drug stability in the lipid vehicle is inadequate (<6 months) to support manufacture and storage of clinical supplies, it may be possible to extemporaneously prepare the dosage form from drug powder at the clinical site using a *powder-in-bottle* approach. During manufacture, weighed amounts of the drug powder, or a simple solid drug-excipient blend, are filled into the required number of suitable containers; a lipid/surfactant/co-solvent blend is prepared and weighed into other containers. At the clinical site, the drug powder and the lipid mixture are then combined as needed for use.

If time allows, use of liquid-filled capsule formulations in clinical trials provides a smoother transition to commercial dosage forms. Soft-gelatin capsules are most commonly used due to their applicability to a wide variety of liquid lipid vehicles (Jimerson, 1986). For most pharmaceutical companies, the manufacture of soft-gelatin capsule products requires the use of third party manufacturers due to the specialized manufacturing equipment. More recently, filling of liquids into hard gelatin capsules has been described, for example, using Capsugel's Li-Caps® system; this is particularly desirable for early drug development when batch sizes are relatively small (Cade et al., 1986). Compatibility of lipid vehicles with hard and soft-gelatin capsules differs, and must be considered (Cole, 1999). Recently, due to concerns with Bovine spongiform encephalopathy/transmissible spongiform encephalopathy (BSE/TSE) and the related trend to avoid animal-based products, there has been some interest in alternative shell materials such as HPMC, which was recently shown to exhibit *in vivo* disintegration times similar to gelatin capsules (Tuleu et al., 2007).