cosolvent systems), but pain on injection or toxicity can be improved. The following examples demonstrate the utility of emulsions:

- Amphotericin B has been formulated as an emulsion by addition of Fungizone to Intralipid 20% and examined clinically. Several reports indicate that the emulsion reduces renal toxicity while maintaining efficacy (Caillot et al., 1992; Chavanet et al., 1992). However, one case report described a patient who had acute renal failure after administration of amphotericin B emulsion (Alford et al., 1994), perhaps due to incomplete incorporation of the drug into the emulsion droplets and precipitation of drug (Davis, 1995).
- Pregnanolone (eltanolone) is a water-insoluble anesthetic that has been in clinical trials as an emulsion developed by Kabi Pharmacia, Sweden. In a clinical study, pregnanolone emulsion appears to induce general anesthesia reliably and smoothly in 13 healthy volunteers, with cardiorespiratory effects similar to other anesthetics (Gray et al., 1992). EEG monitoring indicated the dose inducing 50% of the maximal central nervous system (CNS) depressant effect to be about 0.57 μg/mL (Hering et al., 1995). In a pharmacokinetic and pharmacodynamic study in 6 volunteers, the elimination half-life of pregnanolone was found to be between 0.9 and 1.4 h; hemodynamics and ventilation were only slightly affected (Carl et al., 1990).
- Intraiodol® is an iodinated lipid emulsion taken up by RES tissues, which has led to its clinical examination in 15 patients as a diagnostic agent for computed tomography (CT) of liver (Ivancev et al., 1989).
- Emulsions of perfluorooctyl bromide (perflubron, Imagent®) have been developed by Alliance Pharmaceutical Corp. for imaging of liver by both CT and sonography (Behan et al., 1993). They have also been used as contrast agents for lymph node imaging; subcutaneous dosage of perflubron emulsion into the hands of 18 volunteers led to a dose-related enhancement of CT images of axillary lymph nodes (Hanna et al., 1994). A similar perflubron emulsion, Oxygent®, has been tested clinically as a temporary oxygen carrier at relatively low (1.35–1.8 g perflubron/kg) doses in 57 conscious volunteers and 30 anesthetized surgical patients (Keipert, 1995). Oxygent can be considered a second-generation analog of Fluosol-DA (Table 10.3).
- An emulsion formulation of lipophilic prostaglandin E1 prodrug (AS-013) was evaluated in a clinical study with 10 patients with chronic peripheral aterial occlusive disease (PAOD). The stability of the prodrug was improved relative to the parent drug; the emulsion had acceptable efficacy, and no adverse effects were observed (Matsuo, 1998).

As indicated in Table 10.4, several studies have examined emulsions in decreasing thrombophlebitis and pain on injection of etomidate and diazepam (Von Dardel et al., 1983; Doenicke et al., 1990; Kulka et al., 1993). Intratumoral injection of a bleomycin emulsion has been used in treatment of cystic hygroma and lymphangioma in 27 patients with satisfactory results (Tanigawa et al., 1987).

TOCOSOL® Paclitaxel is a tocopherol emulsion formulation of paclitaxel currently in Phase III clinical trial for the treatment of cancers (Constantinides et al., 2004). The tocopherol-based paclitaxel formulation is prepared by dissolving 10 mg/mL paclitaxel in vitamin E and homogenizing with water and surfactants consisting of TPGS and Poloxamer 407 to yield an emulsion with mean particle size of approximately 100 nm. The use of tocopherol reduces the severe adverse effects related to the use of Cremophor EL in Taxol® (paclitaxel, Bristol-Myers Squibb). The tocopherol-based paclitaxel formulation can be easily administered to patients in a short 15-min infusion compared to 3-hr infusion required by Taxol. Antitumor activity of the formulation has been demonstrated clinically in bladder, ovarian, and non-small cell lung cancers (Hanauske et al., 2005). Paclitaxel is currently marketed as either a solubilized formulation containing polyoxyl 35 castor oil (Cremophor EL) and ethanol, or as a nanosuspension formulation (Abraxane®) containing human albumin.