dosing flexibility. This can be achieved through simple compounding of API in the following dosage forms:

- Extemporaneously Prepared Solution/Suspension (EPS)
- Extemporaneous Dispensation of API in a Capsule

Extemporaneously Prepared Solution/Suspension

Biopharmaceutical properties like poor solubility and permeability are major development issues hindering bioavailability of the NCEs (Venkatesh and Lipper, 2000). In relative terms, the overall rate of absorption of the NCE is affected more frequently by its solubility than its permeability (Hörter and Dressman, 2001). EPS is simplest dosage methodology that can support Phase I objectives. The water-insoluble drug is individually weighed in bottles or other suitable containers. These preweighed doses are reconstituted in the clinic (with an appropriate vehicle specified in the protocol) and dosed immediately. The vehicle composition may solubilize the drug or act as a suspending vehicle. The administering pharmacist in the clinic can also perform dilutions to achieve desired lower doses for a patient. This is typically done in cases where the drug is solubilized in the enabling vehicle. Vehicles used in such procedures include sterile water for injection, dextrose solution, or purified water. Diluted Tween 80 solution and water are most frequently used as a solution for reconstitution. The buffering system for reconstitution can also be used, when investigational compounds have pH-dependent solubility profile. The solubilization of API can be achieved by utilizing numerous techniques such as cosolvents (Yalkowsky and Roseman, 1981a,b) or complex formation (Gupta and Cannon, 2000). Commonly used solvents available to accomplish solubilization are alcohol USP, propylene glycol USP, polyethylene glycol USP (molecular weight 200 and 600), and glycerine USP. These solvents are generally recognized as safe (GRAS) by the FDA and are miscible with water. The level of precedent use in formulation is available in the inactive ingredient guide (Food and Drug Administration, 2006).

The EPS placebo requirement for clinical studies could become an additional challenge in cases where the NCE is colored, bitter tasting, and so forth. In most cases, the reconstituting vehicle alone can be utilized as a placebo. When this is not feasible, bittering agents, buffer salts, and color additives can be used to meet these challenges. This methodology has the advantage of not requiring additional instructions for the clinical pharmacist to prepare the reconstituted solution/suspension for dosing.

The dosing of the NCE immediately after reconstitution helps avoid the need for extensive stability studies. Typically, 12 h stability in solution/suspension (after reconstitution) needs to be assured. The stability data generated for the GMP batch of bulk API supports the regulatory requirement. The GMP requirement for the API dispensing process is much simpler. The analytical resource requirement is limited to identity testing of dispensed API in a bottle. Dose uniformity for this approach could be assured by monitoring individual filling weight through manufacturing process. Overall, this methodology complies with lean manufacturing principles in reducing cycle time to the clinic.

For water-insoluble drugs requiring MDT studies, the dose requirement could run into thousands of bottles. If the company does not wish to invest resources into developing a solubilizing vehicle, then large numbers of bottles can be dispensed using autodose high-precision dispensing technology (Hariharan et al., 2003; Autodose and Powdernium, 2005). This technology allows for simplicity in reconstituting the entire content of the bottle with an aqueous-based vehicle and dosing the entire content of the bottle.

Extemporaneous Dispensation of Active Pharmaceutical Ingredient in a Capsule

Capsule dosage form offers distinct advantages in early phase clinical trials for water-insoluble drugs. The NCE exhibiting color and taste challenges and flexible dosing amount can be easily dispensed in opaque-colored capsules. In the past, use of this dosage form was limited as some