effective on July 15, 1997, a grace period of 2 years, expiring on July 15, 1999, was provided to allow manufacturers to package products in unit-dose blisters and continue to market the product with reduced expiration dating as defined in the guidance. At the same time, the manufacturers were required to initiate and conduct long-term stability studies to establish anew the expiration dating for existing products packaged in unit-dose blisters. Notice should be taken that, for new products containing 30 mg or more of iron per unit dose, the product must be packaged in unit-dose blisters and set up on long-term stability to develop expiration dating before market entry.

Reprocessing and Reworking

Reprocessing and reworking were defined in a draft guidance [7], and though the guidance was later withdrawn by the FDA, it represented the agency's attempts to clarify these terminologies. Reprocessing is the introduction of an in-process material or drug product, including the one that does not conform to a standard or specification, back into the process and repeating steps that are part of the approved manufacturing process. Continuation of a process step after a process test has shown that the step is incomplete is considered to be part of the normal process and is not reprocessing. For most drug products, reprocessing does not require to be described in an ANDA application unless it is known that there is a significant potential for the reprocessing operation to adversely affect the quality attributes of the drug product. Generally, a reprocessed drug product does not require stability testing unless warranted otherwise because of quality concerns.

Reworking is subjecting an in-process material or drug product that does not conform to a standard or specification to one or more processing steps that are different from the manufacturing process described in the ANDA application to obtain acceptable quality in-process material or drug product. In general, reworking operations should be generated postapproval and the ANDA application should be updated through the submission of a PAS, unless reworking operations are anticipated and included at the time of the original ANDA application. Reworking of drug products should be justified by monitoring at least one batch representative of the reworked process under accelerated and/or long-term stability testing [7].

Packaging

Section 505(b)(1)(D) of the Act requires a full description of the facilities and controls used in the packaging of a drug product. Essentially, the Act mandates that the integrity of the container/closure system used in the packaging of a drug product must be maintained during routine packaging operations for marketed products. By definition, the container/closure system means the sum of all packaging components that together protect and contain the drug product. For control of the quality of the container/closure system, the USP has established requirements in the General Chapters <661> Containers and <671> Containers—Permeation. For solid oral dosage forms such as capsules and tablets, the USP requirements essentially relate to moisture permeability, oxygen permeability, and light transmission properties of the container/