

TABLE 7.1
Regulatory Requirements for ANDA and Pre-ANDA Batches

	Batch		
Batch type	Experimental batch	Pilot/confirmatory batch	ANDA batch ("Biobatch")
Batch use	R&D only	Pilot biostudies/trial run before ANDA batch	Submission and any required biostudies
Equipment qualification or calibration	Essential elements (critical processing parameters)	Full	Full
Prevent cross-contamination	Limited	Yes	Yes
Documentation	Abbreviated batch record or laboratory notebook	Full batch record	Full batch record
Batch size	Smallest possible with equipment used	Intermediate for pilot/not less than 100,000 dosage units for confirmatory	Not less than 100,000 dosage units for ANDA pivotal bioequivalence study

EQUIPMENT

Often, research and development (R&D) personnel will argue that because the experimental batch will not be used in any biostudy or other human testing, and because the records and results will not be submitted to the FDA in the ANDA, the experimental batch does not need to be made using calibrated equipment. This can lead to problems further in the development sequence. The results obtained with the experimental batch will be used to make decisions about how to produce the pilot biostudy batch(es), if needed, and the ANDA submission batch(es). Use of unqualified or uncalibrated equipment may lead to erroneous conclusions and the establishment of process parameters that ultimately may not work. The purpose of Installation Qualification, Operational Qualification, Process Qualification, and Calibration are to ensure that the equipment is doing exactly what it is supposed to do. Hence, the essential elements of these processes must be performed on the equipment used to make experimental batches. By essential element, we mean all those functions that are part of the critical processing parameters, such as mixing speed or temperature, whose value has a substantial effect on the quality of the product. For equipment used to manufacture pilot batches to be used in pilot biostudies, complete qualification and calibration are required.

Requirements for prevention of cross-contamination are not the same for experimental batches as for later batches. For batches intended to be administered to humans (research subjects or patients), the sponsor must take steps to ensure that the level of cross-contamination is minimal. Acceptable levels are normally determined