

Alternatively, a critical step may not have any critical process parameters if it can be established that the parameter(s) in question has a NOR that is strictly controlled well-within the PAR.

One way of determining what is a critical process parameter is to begin with the CQAs. Technical experts and engineers from both development and production knowledgeable about the product and the production process should determine the CPP. Quality operations should be involved to verify that the CQA and CPP are properly documented and defensible. A flowchart of the manufacturing process should be made available to all participants. This flowchart should have sufficient detail to readily understand the primary function of each step. Then, each critical product attribute should be evaluated individually to determine what steps may or may not impact that attribute.

Any step or unit operation determined to be critical should be evaluated to determine if it contains one or more critical process parameters. The parameters must have some influence on a CQA to be considered for evaluation as critical. The degree of control over the parameter will determine if it is critical. It is possible to have a critical step that does not contain any critical parameters if control of process parameters is tight. This portion of the analysis requires both knowledge of the process and manufacturing equipment. An example might be a fully automated compression step. The step is critical but complete control over the parameters leads to defined noncritical process parameters. Critical parameters identified during the research and development phase are not necessarily reflective of production scale equipment. The analysis of the process at this level is analogous to a failure modes and effect analysis without estimating frequency of failure or severity of the effect.

Relevant information about any parameters suggested as potentially critical but determined to be non-critical should also be documented.

Example 1-Blending time and tablet lubrication evaluation during R&D

During R&D it is found that the lubricant blending time and the tablet press feed system are critical to tablet hardness. Over-blending of the lubricant leads to soft tablets. R&D conducts a study that defines the NOR limits of the blending step and tablet press feed conditions while still supporting adequate mixing of the lubricant. Blend time and press feed system are critical process parameters.

Defining Ranges for Critical Process Parameters

An understanding of each parameter is necessary before defining a parameter as critical. Parameters may be defined as critical depending on their effect on critical quality attributes, ability to be controlled, and the process design and capability. Process design and process capability are related to the concepts of Edge of Failure (EOF), PAR and NOR.

NOR and PAR values are established during research and development, but may also be further characterized during the manufacturing phase. Some EOF and PAR values may