

The number of lots needed to evaluate the impact of a change should be justified. Justification of fewer lots might be based on demonstrated understanding of the impact of the change, a risk assessment that establishes low risk to quality from the change, or bracketing of the conditions of the change by other conditions that have already been validated.

Regulatory authorities in some jurisdictions may be reluctant to accept certain types of justifications such as bracketing. Continued monitoring of the performance of a well-understood process after completing the scheduled evaluation of the change may also be considered in determining the number of lots to be evaluated.

Table 1. Types of Major Changes and Points to Consider with this Change

Examples of major changes to an established process include, but are not limited to, the following examples. Type of change applies to all (API, DP and packaging) except where noted otherwise.

Table 2. Types of Minor Changes and Points to Consider with this Change

This table provides some examples of minor changes to an established process. Type of change applies to all (API, DP and packaging) except where noted otherwise.

Example 1:

It is proposed that the proven acceptable range (PAR) for a process parameter that impacts a CQA should be tightened. The risk assessment for the CPP should be reevaluated to determine if there is increased risk that a deviation from the normal operating range (NOR) could adversely impact product quality. This change can potentially alter the decision of whether the process parameter is a CPP. Evaluation should consider ability to provide the expected degree of control for the modified parameter.

Example 2:

A new source for the API starting material is being evaluated. Qualification studies may be needed to show that the new supplier's material meets specifications and that the final

API made from it meets specifications. Availability of a supplier assessment and use test results will influence the decision of what validation, if any, is needed for this type of change. Validation may not be necessary if the impurity profile of the final API is unchanged. However if it is necessary to show that the process can adequately control product quality for a different impurity profile, validation is needed.

Example 3:

A significant process change to the API manufacturing process typically prompts activities to qualify the API made by the modified process in the DP manufacturing process. The impact of changes made in the API process may not be revealed in the