

TABLE 3.4
Validation Elements and Acceptance Criteria: Category III

Validation Elements	Acceptance Criteria
Precision	RSD is NMT 2.0%.
Accuracy	Recovery for target analyte is between 98% and 102% for spiked placebo samples at the release tolerances (Q) level.
Method linearity	These acceptance criteria must be met for a five-point concentration method range: <ol style="list-style-type: none"> 1. The correlation coefficient (r) is NLT 0.995. 2. The percent intercept is NLT -5.0% and NMT 5.0%.
Range	The concentration at which the precision, accuracy, and linearity criteria are met. This range should cover from the low concentration end of the stage 3 dissolution test to 120% of the drug release level.
Quantitation limit	The concentration at which the S/N ratio is approximately 10. The quantitation limit should be NMT the reporting threshold defined in ICH Q3B.
Specificity	<ol style="list-style-type: none"> 1. No peak interference in the placebo injection at the retention time of target analyte. 2. The target analyte peak is resolved from the neighboring peaks. 3. The target analyte peak is pure by PDA analysis.
Ruggedness (intermediate precision)	<ol style="list-style-type: none"> 1. The RSD of single determinations (injections) of six preparations under dissolution conditions (second analyst, second dissolution system) must be NMT 3.0%. 2. The RSD for the combined determinations (Analysts 1 and 2) must be NMT 5.0%.
Interference from the automated dissolution sampling system	The percent recovery for the sample collected by the auto-collector must be between 98.0% and 102.0% of the sample collected manually.
Solution stability	The assay of the sample and standard preparations must not change by more than 2.0% in a specified time period at least as long as the time required to perform a typical analysis run (maximum analysis time from sample preparation should be defined in the test method).

All deviations to the validation protocol must be documented and authorized by laboratory management and reviewed and approved by the quality assurance department. These deviations are summarized in the validation report.

VALIDATION PLANNING AND PROTOCOL EXECUTION

Instrumentation Selection

The method validation is considered as a cGMP activity, requiring that the instruments used for the validation activity be fully qualified according to installation qualification, operational qualification, and performance qualification protocols.