

Guidance Number: 80

Figure 1. Regulatory and Non-Regulatory Tests Elimination Process Flow

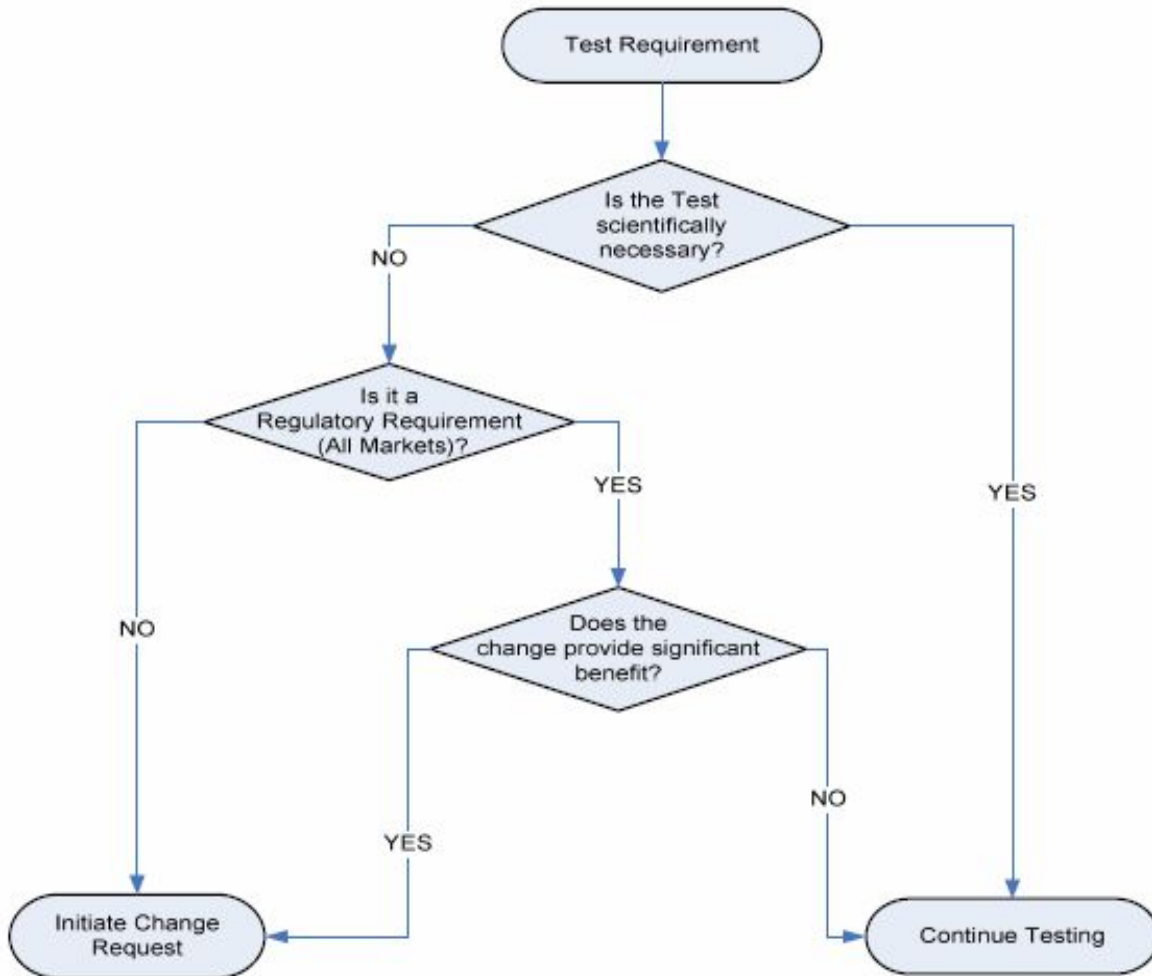


Figure 2. Acceptance of Certificate of Analysis Process Flow

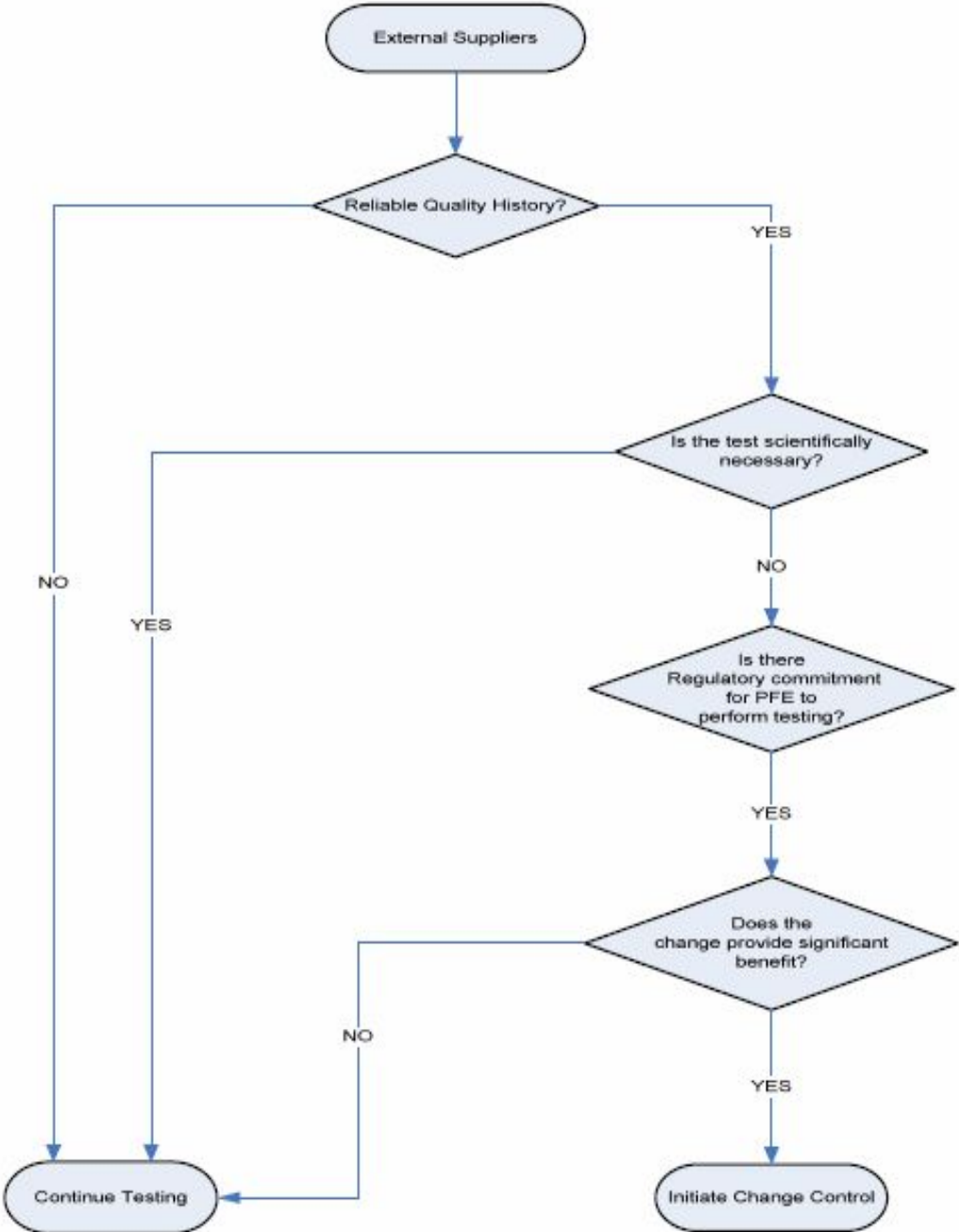


Table 1. Probability, Severity and Detection Ranking Scales

<i>Severity</i>	<i>Description</i>	<i>Probability</i>	<i>Description¹</i>	<i>Detection</i>	<i>Description</i>
1 (MINOR)	Unregistered Raw materials, Non-critical excipients (e.g. filler) or Tertiary packaging components	1 (PROBABLE)	≥10 consecutive lots sourced without issue and Vendor has received an Acceptable rating as a result of most recent audit. Quality Agreement in place.	1 (ALWAYS DETECTABLE)	Multiple in-process and/or finished product tests exist that would identify nonconforming material or the process equipment tolerances are such that nonconforming components would not be machinable.
2 (MAJOR)	Registered starting materials & intermediates, Major excipients (e.g. plasticizer) or Secondary packaging components	5 (OCCASIONAL)	≥3 consecutive lots sourced without issue and/or Vendor has received a Conditionally Acceptable rating as a result of most recent audit. No Quality Agreement, however, cGMP commitment document in place.	2 (SOMETIMES DETECTABLE)	In-process or finished product tests exist that would identify nonconforming material or the process equipment tolerances are such that only components diverging widely from specifications would not be machinable.
3 (SEVERE)	API and critical excipients (e.g. antimicrobial agent) or Primary packaging container and labeling/inserts	10 (FREQUENT)	Sourcing change (new vendor, facility or process) or history of periodic rejects of material based on receipt testing and/or Vendor has received an Unacceptable rating as a result of most recent audit. No Quality Agreement or cGMP commitment document in place.	3 (NOT DETECTABLE)	No in-process or finished product tests exist that would identify nonconforming material or the process equipment tolerances are not such that would prevent nonconforming components to enter the finished product stream.

¹ Represents performance history after material vendor approval process has been completed.

Table 2a. Preliminary Risk Score Evaluation Matrix

↑ Increasing Probability	10	10	20	30
	5	5	10	15
	1	1	2	3
		1	2	3
Increasing Severity →				

Table 2b. Total Risk Score Evaluation Matrix

↑ Increasing Preliminary Risk Score (Severity x Probability)	30*	30	60	90
	20*	20	40	60
	15	15	30	45
	10*	10	20	30
	10	10	20	30
	5	5	10	15
	3	3	6	9
	2	2	4	6
	1	1	2	3
		1	2	3
	Decreasing Detection →			

*Derived using probability score of 10.

Interpretation:

- Scores 1-30 represent acceptable risk
- Scores 45 and all scores (10-90) derived using a probability value of 10 represent unacceptable risk