demonstrated by performing 3 replicates each of three separate sample concentrations (9 determinations) covering the specified range of these procedures.

- Recommended Repeatability Data:
Calculate the result for each replicate. The % RSD for each level should meet the recommended criteria.

- uggested Repeatability Criteria:
Several factors should be considered when selecting criteria: The intended purpose of the test and the expected specification range are important parameters. It is recommended that acceptance criteria be established as recommended in Table 1 and Table 2.

Intermediate Precision:
Intermediate precision expresses "within laboratories" variations (e.g., different days, different analysts and different equipment).

The extent to which intermediate precision may be established depends on the circumstances under which the procedure is intended to be used. It is suggested that sites establish the effects of critical random events on the precision of the analytical test procedure.

Typical variations to be studied include days, analysts, equipment, etc. ICH does not consider it necessary to study these effects individually and this is endorsed by this guideline.

The use of an experimental design (matrix) is considered useful. **Certain markets (i.e. Japan) have more specific requirements for intermediate precision.** To meet intermediate precision requirements for **Japan** for assay and quantitative impurity procedures, it is recommended that the analyses be carried out as prescribed by the method over a minimum of six occasions with at least three analyses per occasion.

An example of such a matrix for Japanese markets is provided in the following table:

	Occurrence #1	Occur #2	Occur#3	Occur #4	Occur.#5	Occur #6
Day	1	1	2	2	3	3
Analyst	1	2	2	1	1	2
Instrument	1	2	1	2	1	2
Column	1	2	1	2	2	1

Analyses can be carried out using either samples spiked at a suitable level(s) and/or representative lots containing a representative amount of impurities. If the representative lots do not contain specified impurities/degradation products, spike studies should be performed. In cases where specified impurities/degradation products are not available a surrogate material such as a compound with similar structure or API may be used to demonstrate precision. In these cases, a rationale for the use of a surrogate should be given.

Recommended Intermediate Precision Data:
Intermediate Precision: Calculate overall % RSD of the multiple occasions. The overall SD or RSD of the multiple occasions should meet the recommended criteria.

methods are recommended to utilize +/- 2.5 standard deviations and Lower risk methods to use +/-2 standard deviations.

The criteria are categorized by actual or anticipated specification limits of the product. Methods that meet these criteria are considered sufficiently accurate and precise to support the product specification limits. More exact criteria for accuracy and precision, based upon process capability indices, can also be used. These criteria define a method as suitable if its mean recovery +/-3 standard deviations (typically intermediate precision) for higher risk methods fall within the specification limits.

Table 2: Recommended Criteria for Precision and Accuracy – Assay Determination

Specification		**Precision**			**Accuracy**
Driver (limit range)		(Repeatability and Intermediate) Higher Risk % RSD	Medium Risk	Lower Risk	% Recovery**
			%RSD	%RSD	
99.0 to 101.0	(+/-	0.3%	0.4 %	0.5	99.5 – 100.5%
1%)					
98.0 to 102.0	(+/-	0.7	0.8	1.0	99.0 to 101.0
2%)					
97.0 to 103.0	(+/-	1.0	1.2	1.5	98.5 to 101.5
3%)					
95.0 to 105.0	(+/-	1.7	2.0	2.5	97.5 to 102.5
5%)					
90.0 to 110.0	(+/-	3.3	4.0	5.0	95.0 to 105.0
10%)					
80.0 to 120.0	(+/-	6.7*	8.0*	10.0*	90.0 to 110.0
20%)					
60.0 to 140.0	(+/-	13.3*	16.0*	20.0*	80.0 to 120.0
40%)					

*If degradation of the material is known to be a concern and/or if this is considered a critical test method, then more conservative criteria are recommended.

** For % Recovery, the amount present in the unspiked sample (if any) should also be taken into account.

To use the tables, first determine the Risk category of the method to determine which Precision column to use.

Next, determine which 'specification driver' is relevant to the material being assayed in order to select the category in the correct row in the above table. Typically, for main analytes, the relevant

