3.10 Trend Analysis

A non-statistical approach to evaluate stability data tendencies over time utilizing techniques such as scatter plots, visual examination, etc. It is intended to detect stability trends that may be indicative of changes in process, methodology or any other parameters that might affect the chemical/physical parameters of the active pharmaceutical ingredient.

3.11 Statistical Analysis

Analysis using formal statistical techniques, e.g. regression analysis, to objectively analyses and compare data.

3.12 Re-test Date

The date when samples of the active pharmaceutical ingredient shall be re-examined to ensure that the drug is still suitable for use.

3.13 Re-test Period

The period of time during which the active pharmaceutical ingredient can be considered to remain within specifications and therefore acceptable for use in the manufacture of a given drug product, provided that it has been stored under the defined conditions; after this period, the batch shall be re-tested for compliance with specifications and then used within a previously defined time period.

4 Responsibilities

4.1 It is the responsibility of each Operation Site to establish stability testing procedures that are consistent with the requirements of this Q&C Procedure and to follow these procedures when conducting stability studies assigned to the site in the Stability Master Plan (SMP).

4.2 It is the responsibility of each Commercial Stability Site to conduct individual stability studies according to the relevant `Integrated Stability Protocols` or local protocols if no `Integrated Stability Protocol` has been issued.

5 Procedure

In case of discrepancies, the regulatory filing/commitments supersede the clauses contained in this Q&C Procedure.

5.1 Introduction

Ongoing surveillance of the stability profiles of commercially available active pharmaceutical ingredients is an integral part of the Company’s quality assurance program. It is essential that stability studies are conducted at Stability Sites as detailed in the SMP issued by the Dossier Management Group (DMG). It is recognized that minor variations may be required as a result of special

5.3.2 Testing Schedule

The schedule below prescribes a varied pull schedule for annual maintenance stability testing dependent on the retest period of the active pharmaceutical ingredient, ranging from 18 to 60 months.

	API Stability Annual Maintenance Stability Testing Schedule				
	25°C/60%RH or 30°C/65%RH				
API retest period ⇒	*18*	*24*	*36*	*48*	*60*
Pull Month *Initial (Note 1)*					
6	*L*				
12	*L*	*L*	*L*	*L*	*L*
18	*L*	*L*			
24		*L*	*L*	*L*	*L*
36			*L*	*L*	*L*
48				*L*	*L*
60					*L*

Note 1Initial results may be taken as the results of the batch release testing only when:

- release testing is completed within 60 days of the study set down date and
- the release methods are identical to those used for stability studies, e.g. assay.

Where the 60-day time limit is exceeded or differences exist between release methods and stability methods, re-analysis by the stability methods shall be conducted at set down.

L = Long Term Stability

25°C/60%RH = Long term storage condition climate I and II, according to ICH
30°C/65%RH = Long term storage condition climate zone III and IV according to ICH

The actual protocol conditions may differ depending on the API characteristics and these conditions will be established based upon the protocol developed to support the first three production batches. Additionally, regulatory commitments may supersede the recommended protocol structure as presented above.

5.3.3 General Requirements for Annual Maintenance Studies on APIs

The general requirements for studies on new APIs (see Section 5.2.4) shall apply to annual maintenance studies, except that the requirement to repeat the initial

