3.14 Bracketing

The design of a stability protocol such that at any point in time only the samples on the extremes are tested, e.g. to evaluate a range of primary package sizes. (See ICH Q1D Bracketing and matrixing designs for stability testing of drug substance and drug products.)

4 Responsibilities

4.1 Registration Officers ROs

The Registration Officer in the Dossier Management Group is responsible for creating and maintaining Stability Protocols and Stability Master Plans for the marketed products and Drug Substances in consultation with the Stability Manager.

4.2 Commercial Site Stability Manager

The Commercial Site Stability Manager or person nominated by the Stability Manager is responsible for

- creating and maintaining protocols that are required for studies that are a result of process validation or process deviations.
- approving Stability Protocols created by DMG ROs
- assuring adequate facilities and resources to execute studies according to the SMP at their site
- acting as the primary contact for the flow of samples and information between international sourcing sites
- ensuring stability set downs according to plans and protocols

4.3 Pack Evaluation Team

The DMG ROs responsible for coordinating Pack Codes and Pack Equivalency Reports (PER) within the Pack Evaluation Team are responsible for supplying other DMG ROs with the relevant information for their Drug Products or Drug Substances.

5 Procedure

5.1 Introduction

The DMG RO in consultation with the Stability Manager or person nominated by the Stability Manager from the Commercial Stability Site shall create the Stability Protocol and Stability Master Plan.

The protocol shall be based upon the ICH Stability Guidelines for new products, WHO Guidelines for stability testing of pharmaceutical products containing well established drug substances in conventional dosage forms and other local guidelines that may be relevant to specific studies.

The Stability Protocol shall include the first or early commercial batches and/or

5.2.10 Document Change History

All changes that have been done at revision of the Protocol shall be listed under this section.

5.2.11 Revision of the Stability Protocol

If the Stability Protocol has had no revisions after two (2) years from the last signature (issue date) of the approved protocol, the DMG RO in consultation with the Stability Manager shall initiate a review of the protocol.

The following changes shall result in the creation of a new version of the Stability Protocol.

- Change in specification
- Change in the tests applied for example a test added or removed
- Condition change
- A new pack code added or an existing pack code removed
- Change in pull times
- A market reporting group is added or removed
- Change in Commercial Stability Site/Testing Site

The first and subsequent versions of the Stability Protocol shall be reviewed by all those required to approve the protocol.

5.3 Information to be included in a Stability Master Plan

In the SMP the DMG RO shall identify the studies required to meet regulatory requirements and GMP compliance and decide upon sample rotation among packaging sites.

5.3.1 Creating the SMP

To create the plan the following information which is contained in the protocol is needed:

- Identification of Drug Product or Drug Substance
- Market Reporting Group
- Study type
- Formulation site. (For liquid products the formulation site is the same as the packaging site)
- Drug Substance Site
- Packaging Site and Pack Details
- Composition code
- Length of study
- Protocol conditions

5.3.2 Studies to put in the SMP

- The first three commercial batches

