4.2.5 Ensuring LIRs are carried out where necessary by initiating them within 24 hours and for ensuring that the Laboratory and/or Quality Manager are notified of any confirmed out of specification results. Ensuring that a DR and/or CR are initiated when required.

4.2.6 Ensuring that analysts who carry out stability testing are appropriately trained.

4.2.7 Reviewing analyst workbooks as per SOP *LAB-025 Laboratory Workbook*.

4.3 The Stability Analysts are responsible for:

4.3.1 Following this SOP to conduct stability studies including initiation, testing and evaluation.

4.3.2 Completing all training required prior to conducting any stability tasks assigned.

4.3.3 Notifying the Stability Team Leader or designee of all questionable, out of trend and out of specification results, within 24 hours of discovery and initiating a LIR when required.

4.3.4 Reviewing the workbook for stability testing performed by other Stability Analysts on request as per SOP *LAB-025 Laboratory Workbook*.

4.4 Business Rules of Conducting Stability Studies

4.4.1 Stability testing is required for, but is not limited to, the following situations, unless there is documented rationale approved by the QA Department for not performing stability testing:

4.4.1.1 Routine required monitoring as per established protocol.

4.4.1.2 Establishment of expiration or reevaluation dates.

4.4.1.3 When required by the Regulatory Authority for the specific market for a change in the Manufacturing process, or change in packaging for regulatory purposes.

4.4.2 Ongoing Stability

4.4.2.1 One representative lot of each product manufactured and packed at the site each year is to be placed on the stability program each year unless there is documented rationale approved by the QA Department for not performing stability testing.

4.4.2.2 If the product is packaged in different container / closure configurations, at least one lot of each configuration should be placed on stability each year.

4.4.2.3 Bracketing and matrixing of stability samples (e.g. different product strengths, different package sizes, or different manufacturing sites) of the same container / closure configuration is permitted.

4.4.3 Production Stability

Testing is required on the product. If stability testing is required a copy should be sent to the Stability Team Leader or designee.

5.1.2.3 When stability testing is required, a Stability Program Protocol must be completed by the QA Designee with details of the change as well as the tests, conditions and time points required. The protocol must be signed by the Stability Team Leader or designee.

5.2 Obtaining Stability Samples

5.2.1 Obtaining Ongoing Stability Samples

5.2.1.1 At the start of each year, the Stability Team Leader / Designee prints out a copy of *Form 735* and records the current year on it.

5.2.1.2 The "Sample Ordered By / Date" on *Form 735* must be filled out when the samples are ordered.

5.2.1.3 The amount of sample required is requested from the appropriate department using *Form 730 Sample Request Form for Stability Program*. The sample amount required is taken from *Form 735*.

5.2.1.4 Ongoing Stability Products can be ordered throughout the year when packaging is completed, unless otherwise specified where a specific batch is requested.

5.2.2 Obtaining Production Stability Samples

The amount of sample required is calculated from the testing and time point requirements as per the Stability Program Protocol created by the QA designee. The sample is requested from the appropriate department using *Form 730 Sample Request Form for Stability Program*.

5.3 Receiving Stability Samples

5.3.1 For Ongoing Stability samples the Stability Team Leader or designee must record the date the samples are received on *Form 735* when the stability samples are delivered to the Laboratory. This form must be reviewed quarterly in partnership with other impacted departments to ensure all required products are on track to be entered into the stability program for the year.

5.3.2 Upon received, all Ongoing and Production Stability sample details must be entered into the Scheduling of New Samples to be Placed On Stability Program Logbook. The logbook typically contains but is not limited to the following headings:

Product Name & Strength
Lot No.
Initial Testing Completion Date

5.7.3 Chemical and Physical Testing must be completed within 30 calendar days from the actual pull date of the sample. "Completed" is the date of acquiring the raw data (e.g. date of HPLC injection).

If testing is not completed within this time frame a DR must be raised to assess the impact of not testing the stability samples within the required time frame.

A planned DR (Deviation Report) can be used to document an action plan and impact assessment on samples that will not be tested within the required timeframe. This can be documented on a monthly basis and can include multiple lots and products.

5.7.4 Microbiological testing must be initiated within 30 calendar days of the actual pull date.

5.7.5 The Stability Analyst must document the testing in the laboratory workbook or any other documents as required as per Good Documentation Practices.

5.7.6 The Stability Analyst must report any result, which is outside of the registration specifications or other specifications outlines in the protocol, or out of trend (even if within specification) to the Stability Team Leader or designee.

5.7.6.1 The Stability Analyst must raise and carry out an LIR (Laboratory Investigation Report) when required in accordance with *SOP LAB-055 Laboratory Results-Out of Specification Investigation*.

5.7.6.2 The Stability Team Leader or designee must carry out the investigation in accordance with SOP LAB-055 Laboratory Results-Out Of Specification Investigation; notify the Laboratory Manager / Quality Authority of any confirmed out of specification results. A DR and/or CR are initiated when required.

5.7.7 On completion of testing, the Stability Analyst must evaluate the results against the registration specification, against any other specifications outlined in the protocol and against that of previous time points. Acceptance criteria for an out of trend result compared to a previous time point are:

For Assay: Variation from previous test point = 4%.

For Dissolution: If initial and second stage test Specifications for dissolution are not met, resulting in a third level of testing, and the product under test has no history of requiring a third level of testing, results shall be considered out of trend.

5.7.8 The Stability Analyst must enter the test results and all relevant information required into Review Page and reports(s) in the Stability Database on completion of testing.

5.7.9 The Stability Analyst should report the results with the same number of decimal places as the specification (unless specified in the reporting criteria from the method; this is normally applied to degradation products).

