changes, i.e., additional stability data added to the stability module for regulatory use. If the Integrated Stability Protocol has had no revisions after two (2) years from the last signature (issue date) of the approved protocol, the Stability Manager shall initiate a review of the protocol to determine if revisions are required. A new version of the protocol shall be issued with appropriate changes or be issued even if the review dictates no changes. The Integrated Stability Protocols for special studies do not require an automatic review every two years, however they should be reviewed and re-issued if they are to be re-used more than 2 years from their previous approval date.

1.7. In the case of studies to support process DR and process validation, the Stability Manager, in consultation with the technical service and local QA Management, shall initiate new protocols for studies that are required because of process DR or process validation programs. It may not be necessary to create a new integrated protocol for each new study set down because of a process DR if an existing integrated protocol meets the requirements of the new study. As with other integrated stability protocols, the release and stability limits, and methodology used in stability testing should be referenced (see sec. 2).

2. Information to be included in an Integrated Stability Protocol

2.1. Site for Study

This section shall identify the Commercial Stability Site, where the stability samples are stored, the testing site(s) and the site(s) that produce the initial results.

2.2. Study Summary

The Study Summary provides the Manufacturing Formulation numbers, their associated Pack Codes, conditions for set down, and each Manufacturing Formulation /Pack Code study length in tabular form. The table, therefore, represents what each marketed product's study length is in its primary pack and the conditions needed for stability to support the expiry life. A statement shall be included in the Study Summary, if secondary packaging is required for stability set downs for products that are, for example, light sensitive. The study length (months) is listed in the conditions columns. The following table can be used as a guide.

Manufacturing Formulation Number/ Article Numbers	Pack Code(s)	Regulatory Designation	25° ± 2° C 60% RH ± 5%	30° ± 2° C 70% RH ± 5%*	40° ± 2° C 75% RH ± 5% (3 early batches)

*This condition is a minimum condition; a higher relative humidity condition may be utilised such as 30°C ± 2°C/ 80% RH ± 5%.

2.3. Schedules

2.3.1. A stability schedule shall be available for new formulated products that include a schedule for the three early commercial batches and for annual maintenance stability. A stability schedule shall be available for mature formulated products that contain an annual maintenance stability schedule.

2.3.2. A stability schedule for the three early commercial batches shall contain the initial and all test points in months for each condition that is applicable for the various Climatic Zones, which the studies support. A two dimensional table with the time pulls and required tests (as identified in the Registered Tests section) shall be constructed for each condition and market. The tables shall be constructed in such a way that the testing required at each time point is clearly identified. The schedule conditions, pull times, and tests shall be based upon the Development batch stability protocol submitted to the various regulatory agencies in order to comply with the ICH

bulk tablets for stability set downs. The simulated pack shall be smaller than the actual drums/containers but shall be of identical or equivalent composition, (e.g., liner and fibre material).
Additional information - Additional information or justifications determined to be necessary shall be provided. This information may relate to the selection of initial results, choice of test laboratories such as contract laboratories or appropriate information that does not suit other sections of the protocol.

2.6. **Sample Plans**

2.6.1. A specific quantity of units is required to complete testing for each Integrated Stability Protocol. That is, an amount is needed for the three early commercial batches and annual maintenance stability batches.

2.6.2. For each Manufacturing Formulation Number and Pack Code combination the number of unit per study and the number of primary packs specified in strips, bottles or units per study shall be listed. The following table can be used as a guide.

Manufacturing Formulation Number / Article Number	Pack Code(s)	Regulatory Designation	Units per Study	Primary Packs per Study

2.6.3. Packs chosen for stability shall be taken in such a way, as they are representative of the entire batch. This does not preclude taking packs from a specific portion of the packaging rim, if these are deemed to be representative of the entire batch.

2.6.4. The specific quantity of tablets, liquid or units shall include overages for OOS testing and microbiological testing as required.

2.6.5. A statement shall be included in the Sample Plans, if secondary packaging is required for stability set downs for products that are, for example, light sensitive.

2.7. **Justification of Stability Protocols**

2.7.1. Study Conditions - a justification shall be provided for the choice of the long term, accelerated, and where necessary the stress conditions based on individual product properties and labelled storage conditions.

2.7.2. Sample Storage - a justification shall be provided for the specific need to store stability samples in terms of orientation (horizontal or vertical) and whether secondary packaging is necessary as for products that are, for example, light sensitive.

2.7.3. Test Points - a justification shall be provided for the choice of the test points. For example, reference shall be made to the ICH guidelines or as specified in regulatory submissions.

2.8. **Changes in the Integrated Stability Protocol**

2.8.1. The Integrated Stability Protocols shall be version controlled.

2.8.2. Changes for each version of the Integrated Stability Protocols shall be listed in a section that documents what changes were made.

3. Summary of Changes

Version #	Revision History
LAB-070	New

End of Procedure

