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1. PURPOSE

This SOP provides a procedure for stability studies of drug products (DPs) at Latitude Pharmaceuticals Inc. (LPI).

2. SCOPE

This SOP applies to stability studies of DPs in pre-clinical to clinical phase 2. It does not apply to registration batches.

3. REFERENCES

- 3.1 ICH Q1A (R2)
- 3.2 LPI-SOP-102 "Analytical Method Validation, Verification, and Transfer"
- 3.3 LPI-SOP-409 "Deviations: Notification, Handling, and Investigation"
- 3.4 LPI-SOP-411 "Investigation of Out-of-Specification Results"
- 3.5 LPI-SOP-412 "Reporting Analytical Results"
- 3.6 LPI-SOP-415 "Preparation of Certificate of Analysis"
- 3.7 LPI-SOP-418 "Investigation of Questionable Analytical Results"
- 3.8 LPI-SOP-101 "Management and Testing of GLP/GMP Samples"

4. ATTACHMENTS

Attachment A: Stability Protocol Format

Attachment B: Stability Report Format

Attachment C: Process Flow

Attachment D: Stability Study Pull Checklist

5. ABBREVIATIONS / DEFINITIONS

Accelerated Testing: Studies designed to increase the rate of chemical degradation or physical change of a drug product by using exaggerated storage conditions as part of the formal stability studies. Data from these studies, in addition to long term stability studies, can be used to assess longer term chemical effects at non-accelerated conditions and to evaluate the effect of short-term excursions outside the label storage conditions such as might occur during shipping. Results from accelerated testing studies are not always predictive of physical changes.

Container Closure System: The sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components, if the latter are intended to provide additional protection to the drug product. A packaging system is equivalent to a container closure system.

Expiration Date: The date placed on the container label of a drug product designating the time prior to which a batch of the product is expected to remain within the approved shelf life specification if stored under defined conditions, and after which it must not be used.

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Formal Stability Studies: Long term and accelerated (and intermediate) studies undertaken on primary and/or commitment batches according to a prescribed stability protocol to establish or confirm the re-test period of a drug substance or the shelf life of a drug product.

Impermeable Containers: Containers that provide a permanent barrier to the passage of gases or solvents, e.g., sealed aluminum tubes for semi-solids, sealed glass ampoules for solutions.

Intermediate Testing: Studies conducted at 30°C/65% RH and designed to moderately increase the rate of chemical degradation or physical changes for a drug product intended to be stored long term at 25°C.

Long Term Testing: Stability studies under the recommended storage condition for the re-test period or shelf life proposed (or approved) for labeling.

Semi-Permeable Containers: Containers that allow the passage of solvent, usually water, while preventing solute loss. The mechanism for solvent transport occurs by absorption into one container surface, diffusion through the bulk of the container material, and desorption from the other surface. Transport is driven by a partial-pressure gradient. Examples of semi-permeable containers include plastic bags and semi-rigid, low-density polyethylene (LDPE) pouches for large volume parenteral (LVPs), and LDPE ampoules, bottles, and vials.

Shelf Life (also referred to as expiration dating period): The time period during which a drug product is expected to remain within the approved shelf life specification, provided that it is stored under the conditions defined on the container label.

QC: Quality Control.

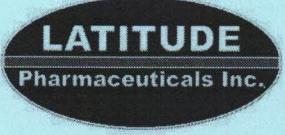
SOP: Standard Operating Procedure.

6. PROCEDURE

6.1 Roles and Responsibility

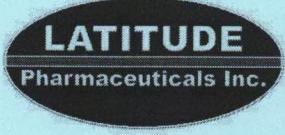
Roles	Responsibilities
Analyst	<ul style="list-style-type: none"> • Logs the usage of stability chamber per LPI-SOP-603. • Pulls samples from stability chambers and record samples in the logbook form # LPI-SOP-101 Attachment A. • Requests related forms or datasheets from QA/DCU and gives the forms/datasheets to the analysts for recording analysis. • Ensures that stability studies are conducted in accordance to the stability protocol and in compliance with GLP/GMP requirements. • Performs testing for stability samples in accordance to the approved protocol. • Informs direct supervisor for any out-of-specification, questionable results, or system suitability failure. • Prepare stability summary in accordance to the project's respective protocol.

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Roles	Responsibilities
Designated Analyst	<ul style="list-style-type: none"> • Receives samples and logs into LPI-SOP-101 Attachment A. • Informs stability supervisor on scheduled stability interval tests, who will then assign an analyst to pull samples from stability chambers per stability protocol, and then the analyst logs in the sample tracking log per LPI-SOP-101. • Communicates to the supervisor of the stability and QA when a non-compliance issue exists or occurs during conducting testing of the stability samples and may impact the quality or integrity of a study or studies. • Monitor stability chambers to ensure proper functioning and take appropriate actions when stability chambers fail. • Reviewed logbook LPI-SOP-101 Attachment A to ensure that samples have been recorded in logbook form # LPI-SOP-101 Attachment A at each test interval.
Supervisor / Designee	<ul style="list-style-type: none"> • Serves as a point of contact for Principle Investigators, Management, and/or clients for information related to the storage and conduct of stability studies. • Writes stability protocol, report, and reviews stability test results, and trending. • Assigns testing to analysts. • Ensures the analysts are trained. • Ensures the analytical instruments and methods have been adequately qualified before use. • Ensures all tests are conducted in accordance to stability protocol. • Serves as point of contact to clients on any issues or updates. • For OOS investigation, works with QA to initiate investigation in accordance to LPI-SOP-411. • For investigation of questionable results, works with QA to initiate investigation in accordance to LPI-SOP-418. • Writes deviation if a deviation occurs in relation to the stability protocol in accordance to LPI-SOP-409. • Reviews, approves, or rejects the COA. • Periodically reviews logbook to ensure sample logs are up to date.
Quality Assurance (QA)	<ul style="list-style-type: none"> • Reviews and approves stability protocol. • Verifies the stability pull schedule at each test interval. • Reviews and releases or rejects the summary report. • Works with supervisor for all investigations (OOS, questionable results).
Document Control Unit (DCU)	<ul style="list-style-type: none"> • Issues forms / datasheets to the supervisor or his designee. • Creates Stability Binder per Section 6.2.2

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6.2 Sample Receiving and Study Initiation

- 6.2.1 Project leader or a designee will write a stability protocol and has it approved. The stability program will be designed specifically for the drug product in the individual protocol.
- 6.2.2 The stability study will not start unless a signed and approved protocol is available.
- 6.2.3 The samples to be placed on stability will be received, logged in form LPI-SOP-101 Attachment A, and stored per LPI-SOP-101 before the initiation of stability study.
- 6.2.4 Prior to placement into the chamber, the samples will be labeled with following information: stability protocol number, material information (including container closure information, e.g., vials, ampules, etc.), lot number, storage condition (and orientation if applicable). It is recommended to have samples stored in both normal and inverted position (worst case).
- 6.2.5 Once the samples have been placed in the appropriate chambers, the analyst will log the sample information onto additional LPI-SOP-101 Attachment A for sample tracking and use this form to track each stability pull, then file in the stability sample logbook.
- 6.2.6 Only release samples can be stored in stability chambers for stability studies. Both study supervisor and QC will maintain the pull schedule to aid the management of sample pulling and study planning. The supervisor will work with the analyst to pull samples for testing. The analyst is responsible for logging the samples in the logbook form LPI-SOP-101 Attachment A. QC personnel will review the logbook to ensure samples have been properly logged in LPI-SOP-101 Attachment A.

6.3 Storage Conditions and Test Frequency

The storage condition and lengths of the studies chosen should be adequate to cover storage, shipment, and subsequent use (product shelf life). Storage conditions are evaluated based on the product and its packaging container.

In general, studies should be evaluated for physical, chemical, biological, and microbial stability. **Table 1** lists general case of storage conditions, minimum testing period, and test frequency. The stability storage and frequency testing can be specified in the individual study protocol.

The time 0 testing is performed in according to study protocol for use as baseline or control samples. Alternately, the release data from the drug product's Certificate of Analysis (COA) or the COA values can be used for time 0.

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Table 1. General Case Storage Conditions

Storage	Condition	Minimum time period covered by data at submission	Test Frequency
Long term*	25°C ± 2° / 60%RH ± 5%RH Or 30°C ± 2° / 65%RH ± 5%RH	12 months	Year 1: every 3 months Year 2: every 6 months Year 3 and after: Yearly
Intermediate**	30°C ± 2° / 65%RH ± 5%RH	6 months	Minimum 4 time points (e.g., 0, 6, 9, 12 months) when testing is performed due to significant changes in the accelerated condition.
Accelerated	40°C ± 2° / 75%RH ± 5%RH	6 months	Minimum 3 times points (e.g., 0, 3, 6 months)

*: It is up to the stability supervisor or client to decide whether long term stability studies are performed at 25°C ± 2° / 60%RH ± 5%RH or 30°C ± 2° / 65%RH ± 5%RH.

**: If 30°C ± 2°C/65% RH ± 5% RH is the long-term condition, there is no intermediate condition.

6.3.1 DPs Packaged in Impermeable Containers

There is no concern with potential water or solvent loss for DPs packaged in impermeable containers since these containers provide a permanent barrier to passage of moisture or solvent. Therefore, stability studies can be conducted under any controlled or ambient humidity condition.

6.3.2 DPs Intended for Storage in Refrigerator

Table 2 lists storage conditions for DPs intended to store in refrigerator.

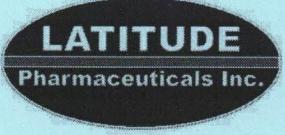
If the drug product is packaged in a semi-permeable container, appropriate information should be provided to assess the extent of water loss.

If significant change occurs between 3 and 6 months' testing at the accelerated storage condition, the proposed shelf life should be based on the real time data available from the long-term storage condition.

Table 2. Storage Conditions for DPs Intended for Storage in Refrigerator

Storage	Condition	Minimum time period covered by data at submission	Test Frequency
Long term	5°C ± 3°C	12 months	Year 1: every 3 months Year 2: every 6 months Year 3 and after: Yearly
Accelerated	25°C ± 2°C / 60%RH ± 5%RH	6 months	Minimum 4 time points (e.g., 0, 6, 9, 12 months) when testing is performed due to significant changes in the accelerated condition.

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6.3.3 DPs Intended for Storage in Freezer

Table 3 lists storage conditions for DPs intended for storage in the Freezer.

In the absence of accelerated conditions, testing on single batch at elevated temperature (e.g., $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$ or $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$) should be evaluated to address the effect of short-term excursions outside the proposed label storage condition.

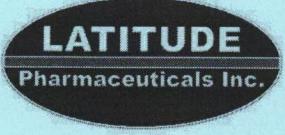
Table 3. Storage Conditions for DPs Intended for Storage in Freezer

Storage	Condition	Minimum time period covered by data at submission	Test Frequency
Long term	$-20^{\circ}\text{C} \pm 3^{\circ}\text{C}$	12 months	Year 1: every 3 months Year 2: every 6 months Year 3 and after: Yearly

6.4 Sample Pulling and Testing

- 6.4.1 Stability storage and testing will be conducted under an approved protocol only.
- 6.4.2 During the study, any change or amendment to an approved protocol will go through review, approval process, and supersede the previous version of protocol once in effect.
- 6.4.3 Through the course of the study, the study supervisor and stability coordinator will ensure samples are properly documented on LPI-SOP-101 Attachment A.
- 6.4.4 The designated analyst will work with analyst to pull samples on the scheduled date. A designated analyst will log out the sample tracking log per LPI-SOP-101, and stability chamber log per LPI-SOP-603. Unless stating in the protocol, the tolerance for variation from the scheduled pull date is ± 3 days to accommodate weekend pulls. For samples older than a year, the tolerance for variation from scheduled pull date is ± 7 days. Other tolerance for variation can be specified on individual study protocol with justification.
- 6.4.5 The designated analyst will inform the study supervisor for upcoming pulls. Supervisor then assigns an analyst to pull samples and record samples in LPI-SOP-101 Attachment A and assigns testing to the analysts. The supervisor or her designee requests the forms necessary for recording the tests.
- 6.4.6 After samples were pulled from storage per stability protocol, at least one testing should be initiated within 3 business days from the sample pull date. The analyst should complete all the tests within 30 days from the pull date, unless otherwise stated in a protocol. Once testing is complete, the

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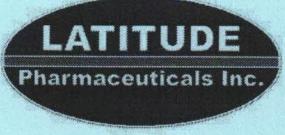
analyst submits related attachments and data sheets to QC supervisor or designee for review. Any deviations related to testing (for example, delay in testing >30 days) will be documented as protocol deviation or per LPI-SOP-409.

- 6.4.7 The analysts will perform the test per the approved stability protocol provided by his/her supervisor and by QA. Document testing in the approved forms or datasheets associated with the test. The data & results will be reviewed by the analyst's supervisor or a designee.
- 6.4.8 After the data and test results have been reviewed and signed off (Section 6.4.7) the designated analyst will prepare the COA summarizing the test results and submit the COA with the reviewed data to the supervisor for approval unless otherwise stated in the protocol.
- 6.4.9 The supervisor or designee reviews, approves or rejects the COA.
- 6.4.10 The supervisor or designee submits the stability summary with the associated reviewed data packages to QA for releasing.
- 6.4.11 The QA reviews and releases the stability summary. The original COA is filed in the "Stability Binder." Copy of COA is scanned and saved in LPI server as backup document.
- 6.4.12 Study supervisor and/or designated personnel will perform and ensure tracking and trending of stability results.

6.5 Test Methods and Specification

- 6.5.1 Stability samples, generally, will be evaluated for physical, chemical, biological, and microbial stability per DP specification as specified in the protocol. Stability studies will include testing of those attributes of the drug product that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy. Testing will cover, as appropriate, physical, chemical, biological, and microbial attributes, which are defined in the study protocol.
- 6.5.2 It is recommended to use USP methods for testing when it is possible. The USP methods are required to verify for the DP under the actual condition of use. Refer to LPI-SOP-102 for information on verification of USP methods.
- 6.5.3 For methods developed at LPI, the methods are required to be qualified before use and are required to completely validated by clinical phase 3. Refer to LPI-SOP-102 for information on validation of analytical methods developed at LPI or as required by the client/sponsor. It is recommended to validate the stability-indicating method before use.

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6.6 Evaluation of Stability Data

- 6.6.1 The purpose of a stability study is to establish an expiration date applicable to all future batches manufactured under similar circumstances. The test duration should bracket the expiration date.
- 6.6.2 For data that may show slight degradation and variability, the retest date can be assigned without formal statistical analysis. For out-of-specification or questionable results, report to the study supervisor, who will evaluate to determine the course of action that was based on stability trending results or chemical knowledge. For stability related issues, an OOS investigation is not required. For questionable analytical results, an investigation is conducted in according to LPI-SOP-418. If an OOS result is not related to chemical stability, an investigation is conducted according to LPI-SOP-411.
- 6.6.3 The relationship of degradation with time can be statistically analyzed to extrapolate a retest date, such tests including linear regression, quadratic or cubic function of an arithmetic or logarithmic scale. Any evaluation for a retest date should include assay and related substances and other appropriate attributes.

6.7 Completion of the Study

Upon termination or completion of the stability study, the excess materials within the chambers will be removed and handled as outlined in the protocol or by client's written request in the forms of memo or email. Client's request will be filed with the "Stability Binder" for references. The sample tracking log will be completed and filed with the Stability Binder. The completed Stability Binder will be returned to QA for archiving.

6.8 Disaster Recovery

Any unforeseen event (natural disaster or unplanned accident) that could destroy samples or significantly alter the storage conditions of the samples to the point where the study would be negatively impacted. After the disaster, stability storage chambers should be assessed to determine if they can function properly. If stability chamber is out of tolerance, the samples will be transferred to another storage chamber of the same tolerance. If another storage chamber does not have the same tolerance, the samples will be stored under a condition that has minimal impact on the study. The study supervisor and QA will be informed. The study supervisor will assess the potential impact of the studies and notify the client.

6.8.1 Stability Chamber Failure

A mechanical malfunction in which the chamber cannot meet the tolerances specified in the study protocol.

If there is available stability chamber of the same tolerance, designated analyst moves all samples to that chamber, notifies study supervisor and QA, and add notes to the sample tracking log.

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If stability of the same tolerance is not available, the samples will be stored under a condition that has minimal impact on the study and then notifies the study supervisor and QA.

6.8.2 Power Failure

A lack of sufficient electricity from the electrical supplier to properly operate the stability chambers.

If there is a power outage, the battery powered data logger will capture the impact on the storage condition.

6.8.3 Natural Disaster

Any natural phenomenon (i.e., fire, flood, tornado) that does substantial damage to the building in which the stability chambers are housed will be documented.

In the event natural disaster damage stability chamber, the designated analyst will attempt to recover as many samples as it is safe to do so, then informs study supervisor and QA.

6.9 Documentation

Documents required for stability studies include stability protocol, forms or datasheets, result summary with stability trending in Excel spreadsheet, and COA at each test interval. A final stability report is written at the end of the stability studies. Format for stability protocol and report are in Attachment A and Attachment B, respectively.

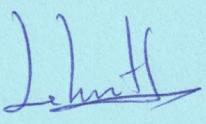
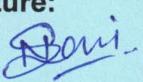
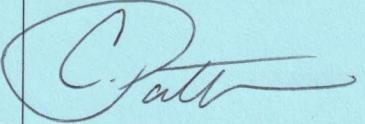
6.10 Deviation

Any deviation will be documented in accordance to LPI-SOP-409.

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7. APPROVALS

Author Name: Ella He	Author Title: QC Scientist	Author Signature: 	Date: 12/08/2025
Reviewer Name: Neha Soni	Reviewer Title: QA/QC Manager	Reviewer Signature: 	Date: 12/09/2025
Approver Name: Carl Patterson	Approver Title: Director of Quality	Approver Signature: 	Date: 12/09/2025

Revision No.	Summary of Changes	Effective Date	Author
000	New document	09/30/2020	Daisy Khuu
001	Updated format. Removed reference to stability study binder and stability coordinator.	09/02/2022	Andrew Kondan
002	Updated section 6.4.6 to change 2 working days to 2-3 business days to prevent deviations caused by weekends and holidays. References to LPI-FM-112 have been changed to mention LPI-SOP-101 Attachment A for sample pull records. Included Attachment D for a stability pull monthly checklist.	02/10/2025	Viet Ngo
003	Section 3: Updated format as per current template. Section 5: Added abbreviations of QC and SOP for clarity. Section 6.4.6: Clarified sample pull date and testing completion window. Section 6.4.8: Added "unless otherwise stated in the protocol" to add flexibility. Section 6.4.9 and 6.4.10: Added designee to add back up if the supervisor is not available. Section 6.4.11: Updated "QA manager" to "QA" to add flexibility.	07/11/2025	Neha Soni
004	Section 6.4.6: Clarify the protocol deviation procedures.	12/11/2025	Ella He

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ATTACHMENT A: STABILITY PROTOCOL FORMAT

The protocol should generally contain the following structure:

- Protocol number
- Title of the study
- Name and contact of client, study supervisor, and name and address of additional test facility.
- Proposed study starts and completion dates
- Scope
- Reference
- Attachments (include sample pulling schedule form)
- Definitions
- Roles & Responsibilities
- Materials & Equipment
- Background/Introduction
- Table Summary of Tests, Test Methods, and Test Specifications
- Procedure (test DP information, storage condition, test duration & frequency, numbers of samples pulled per interval, disaster recovery)
- Deviations
- Documentation

ATTACHMENT B: STABILITY REPORT FORMAT

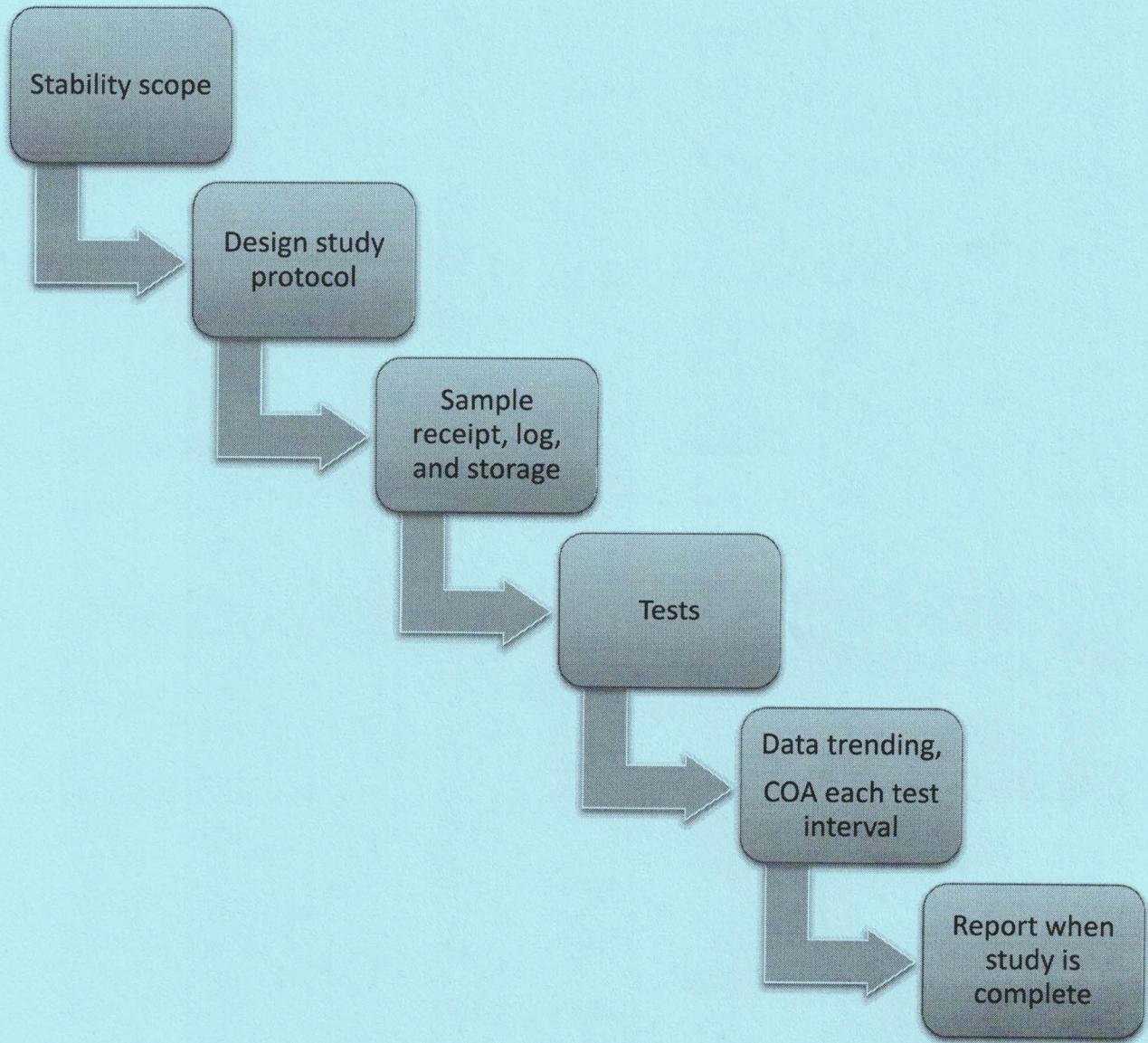
The report should contain the following structure

- Summary
- Summary table
- Reference
- Attachments (recommends attaching the chromatograms of 0 time, 3 months, 6 months, 12 months and last time points, along with the stability trending charts).
- Materials & equipment
- Results
- Deviations
- Conclusion with recommendation retest date if applicable

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ATTACHMENT C: PROCESS FLOW



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ATTACHMENT D: STABILITY STUDY PULL CHECKLIST

Year: _____

Month	Checked (Initial/Date)	Verified (Initial/Date)
January		
February		
March		
April		
May		
June		
July		
August		
September		
October		
November		
December		

QA Reviewed by: _____

Date: _____

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