SOP Title: **Biopharmaceutical Development Program Stability Management**

SOP Number: **22502**

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1. PURPOSE

This SOP describes the procedure for stability management for CGMP products produced by the Biopharmaceutical Development Program (BDP).

2. SCOPE

This procedure applies to Process Analytics/Quality Control (PA/QC) and Biopharmaceutical Quality Assurance (BQA) staff involved in stability studies. It pertains only to real-time studies for the first three lots of material produced by a particular manufacturing method. Accelerated and Infusion studies are not covered in this SOP.

3. RESPONSIBILITIES

3.1 Director, Process Analytics/Quality Control (PA/QC)

- Defines this procedure.

3.2 PA/QC Management

- Reviews the data and documentation of the results of this procedure.
- Investigates any Out-of-Specification or unexpected results.
- Summarizes the data and submits the reports for review and approval

3.3 Stability Coordinator

- Completes the request for testing.
- Summarizes the data and submits the reports for review and approval

3.4 Quality Assurance Management

- Reviews interim/final stability reports.
- Provides quality oversight for this procedure.

4. STABILITY PROTOCOLS

4.1 cGMP products produced by the BDP are monitored for real-time stability following an approved stability protocol.

4.2 The stability protocol specifies the testing required, the specifications, and the frequency of testing.

4.3 Stability protocols assess the stability of BDP products over a predetermined period of time. It is an assessment of the physical and functional integrity of the product. The frequency of testing typically follows the recommendation in ICH Q1A Stability Testing of New Drug Substances and Products (i.e., 0, 3, 6, 9, 12, 18, 24 months and annually thereafter). Other frequencies may be acceptable, with team agreement as documented during protocol approval. The protocol may be revised to extend the duration of the testing, depending on the duration of the clinical trial(s) using the product.

4.4 Stability Study changes follow the requirements in **SOP 22529 Origination, Implementation, and Maintenance of Stability Protocols and Reports.**Refer to **SOP 22529 - Origination, Implementation, and Maintenance of Stability Protocols and Reports** for more information on stability protocols.

5. STORAGE EQUIPMENT/TEMPERATURE RANGES

There are five defined temperature ranges available for storage of stability samples.

- Room temperature (Ambient, 15 to 30°C)
- 2 to 8°C
- -10 to -20°C
- -20 to -40°C
- ≤ -70°C
- LN_2 Vapor Phase

6. REFERENCE STANDARDS

Refer to **SOP 22716 – BDP Reference Material Management**.

7. PROCESSING OF STABILITY SAMPLES

7.1 Samples for stability testing are pulled upon completion of manufacture and placed at the specified storage temperature by the Manufacturing Fill/Finish Group (i.e., the storage temperature at which the clinical lot is stored). These samples will be inventoried by either Materials Management and Inventory Control (MMIC) OR PA/QC Accessioning.

7.2 If stability samples are inventoried by MMIC: Samples are withdrawn from MMIC per **SOP 20303 - CGMP Product Accountability** by the Stability Coordinator.

7.3 Stability samples will be input into PA inventory system per **SOP 22907 - Sample Accessioning and Trafficking**. PA/QC Accessioning personnel place samples into approved storage location per the stability protocol and enter the information in the Stability FreezerWorks.)

7.4 Stability information (including Product Name, Lot Number, Production Date, and Time Points) are entered by the Stability Coordinator into “Stability Testing” database located on BDP Public, in the PA Stability folder.

7.5 When samples are pulled for stability testing, always check to make sure there is enough material for the next stability time point. Otherwise, check with PA/QC Department Head.

8. TESTING OF SAMPLES AT PRESCRIBED INTERVALS

8.1 Prior to the first of every month, a list of products having a time point during that month is generated from the “Stability Testing” database for the coming month.

8.2 Test Requests for products is completed per **SOP 22002 - Request for Quality Control Testing** (one for each assay on the stability protocol). The “results needed by” line on the test request is the exact time point (i.e., end of the month) so that analysts may schedule testing to meet or coincide with the time point, if feasible.

8.3 Complete an Inventory Withdrawal record for each product and approved reference standard(s), then submit it to PA/QC Accessioning staff with test requests and record using **Form 20303-01** for each product lot, including any reference materials and standards required. The Stability FreezerWorks sample database is updated accordingly and a copy of the database record is printed for inclusion in the appropriate hard-copy inventory catalog for each stability storage location. The hard-copy inventory catalogs are held in the Accessing office.

8.4 Test requests should be submitted immediately prior to or at the beginning of the test month, whenever possible.

9. STATUS AND FOLLOW-UP

9.1 A copy of each test request is inserted in the Accessioning QCTR files and used as a placeholder until the test is completed and reviewed data is available.

9.2 A status spreadsheet is maintained of outstanding and planned stability testing by the Stability Coordinator.

10. DOCUMENTATION AND RECORDS

10.1 QC data is found either in the BDP App or in the QCTR Final folder on the QC Test Requests drive.

10.2 A general summary of the reported time-point, if the product met the required specifications, and the next scheduled time-point is included in the report. Information regarding the report is found in **SOP 22529 Origination, Implementation, and Maintenance of Stability Protocols and Reports.**

10.3 An individual time-point table is also included in the report.

10.4 A full table of data is maintained in the report. This table summarizes the testing results “to date” and allows for rapid visual trend analysis on the results of each assay performed.

10.5 Reports are generated upon completion of individual time points and distributed. See **SOP 22529 Origination, Implementation, and Maintenance of Stability Protocols and Reports.**

10.6 Reports may also be distributed to NCI/CTEP, clinical pharmacies, other government agencies or institutes, and other clinical sites as required.

11. REFERENCES AND RELATED DOCUMENTS

Document Number	Title
Q1A (R2)	ICH Guidance for Industry "Stability Testing of New Drug Substances and Products." November 2003
Q1E	ICH Guidance for Industry Q1E "Evaluation of Stability Data." June 2004
Q5C	ICH Guidance for Industry Q5C "Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products." July 1996
20303	CGMP Product Accountability
20303-01	MMIC CGMP Manufacturing Product Inventory
22002	Request for Quality Control Testing
22529	Origination, Implementation and Maintenance of Stability Protocols and Reports
22716	BDP Reference Material Management
22907	Sample Accessioning and Trafficking