Frederick National Laboratory for
Cancer Research, Frederick, MD

BDP BD

Biopharmaceutical Development Program

Standard Operating Procedure

Title: Biopharmaceutical Development Program Stability Management

SOP Number: 22502

Revision Number: 03

Supersedes: Revision 02

Effective Date: **APR 15 2019**

Originator/Date: [redacted]

Approval/Date:

Approval/Date:

Table of Contents

1.0 Purpose

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

2.0 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.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted]

3.0 Authority and Responsibility

3.1 The Director, Process Analytics/Quality Control (PA/QC) has the authority to define this procedure.

3.2 The PA/QC Stability Coordinator is responsible for the performance of this procedure.

3.3 PA/QC is responsible for training laboratory personnel and documenting this training to Biopharmaceutical Quality Assurance (BQA).

3.4 PA/QC management is responsible for reviewing the data and documentation of the results of this procedure. This includes interim stability reports, final stability reports, and "Out of Specification" (OOS) investigations.

3.5 BQA management is responsible for reviewing interim/final stability reports and quality oversight of this procedure.

4.0 Stability Protocol

4.1 CGMP products produced by the BDP will be monitored for real-time stability following an approved stability protocol.

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

4.3 Stability protocols assess the stability of BDP products for a minimum of two years. It is an assessment of the physical and functional integrity of the product. The frequency of testing is typically at 0, 3, 6, 9, 12, 18, and 24 months. The period of stability testing that protocols cover will be extended for the duration of clinical trials that the products are used.

4.4 With documented approval, the stability study may be modified, terminated early, put on hold, or extended for a longer time-period.

4.5 Refer to ***SOP 22529 - Origination, Implementation, and Maintenance of Stability Protocols*** for more information on stability protocols.

5.0 Storage Equipment/Temperature Range

There are five defined temperature ranges available for storage of stability samples within the PA/QC Accessioning Area [redacted]).

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

6.0 Reference Standards

6.1 Reference Standards will be approved by Quality Assurance before execution of this procedure per ***SOP 22716 – BDP Reference Material Management***.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

7.0 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 will be 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 will place samples into approved storage location in [redacted] per the stability protocol and enter the information in the Stability FreezerWorks "SkyPilot" database ([redacted]

7.4 Stability information (including Product Name, Lot Number, Production Date, and Time Points) will be entered by the Stability Coordinator into "Stability Testing" database located on BDP Public ([redacted]).

8.0 Testing of Samples at Prescribed Intervals

8.1 Before the first of the month, a list of products having a time point during that month will be generated from the "Stability Testing" database.

8.2 Test Requests for products will be 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 form will be 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 [redacted] (Accessioning office).

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

9.0 Status and Follow-up

9.1 A copy of each test request will be 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.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted]

10.0 Documentation

10.1 QC data will be kept in project specific electronic stability folders in the [redacted] folder for the appropriate product and lot number.

10.2 A full table of data will be maintained (**Attachment I**). This table summarizes the testing results "to date" and allows for rapid visual trend analysis on the results of each assay performed.

10.3 An individual time-point table will also be written to the project folder (**Attachment II**).

10.4 A cover memo to the Branch Chief, Biological Resources Branch, will be generated to provide a general summary of the reported time-point, if the product met the required specifications, and the next scheduled time-point. (**Attachment III)**

10.5 Reports will be generated upon completion of individual time points and distributed to (at a minimum): BDP Project File, Principal Investigator(s), BDP QA, BRB (or other NIH) Representative, and the BDP Project Scientist.

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

10.7 A final report will be written after the last time-point is complete and provided to (at a minimum): BDP Project File, Principal Investigator, BDP QA, BRB (or another NIH) Representative, and the BDP Project Scientist.

11.0 References

11.1 ICH Guidance for Industry Q1A (R2) "Stability Testing of New Drug Substances and Products." November 2003.

11.2 ICH Guidance for Industry Q1E "Evaluation of Stability Data." June 2004.

11.3 **SOP 20303** *CGMP Product Accountability*

11.4 **SOP 22002** *Request for Quality Control Testing*

11.5 **SOP 22529** *Origination, Implementation and Maintenance of Stability Protocols*

11.6 **SOP 22716** *BDP Reference Material Management*

11.7 **SOP 22907** *Sample Accessioning and Trafficking*

12.0 Attachments

12.1 **Attachment I** Table 1: Results for Product

12.2 **Attachment II** Results for Product

12.3 **Attachment III** Sample Cover Memo

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted]

Attachment I

Table 1. Results for Product XYZ, Lot #12346, Time 0 through 24 Months
Production Date: **XX/XX/XX**

Test	Specification	Time Point						
		0 Months XX/XX/XXXX	3Months XX/XX/XXXX	6Months XX/XX/XXXX	9Months XX/XX/XXXX	12Months XX/XX/XXXX	18Months XX/XX/XXXX	24Months XX/XX/XXXX
TBD	TBD	Pending QC-XX)()()(	NA	NA	NA	NA	NA	NA
TBO	TSO	Pending QC-XXXXX	NA	NA	NA	NA	NA	NA
TSO	TSO	Pending OC-XXXXX	NA	NA	NA	NA	NA	NA
TSO	TSO	Pending QC•XXXXX	NA	NA	NA	NA	NA	NA
TBD	TSD	Pending QC-XXXJO(	NotRequired	NotRequired	NotRequired	NA	NotRequred	NA

Time p01nt ha snd been reached.

Reviewed and approved by:_____ Date:_____
B1opl'larmaceutlca1Qualtiy Control

[redacted] Confidential

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Attachment II

Results for Product XVZ, Lot #12345

Vialed XXJXX/XX

National Cancer Institute-Frederick, Frederick, MD

Blooharmaceutical Develoomeot Proaram

Stability Study Specific21ion Form					
Dt tription: Product XYZ	Datt'of Mnnufnthr t: XXDOOXX		llDP Lot No.: 12345	V, ndor Lot No.: XXXXX	
TimePoint: XX-Month	Storage Conditions; XA" C		Study No.: SP-XXX		
Te,t	Me,th d	Testing Lab	Liu ib / Spu: ificatioru	R-. ulb	Pa, .tF ail
I. TBD	mo	BQC QC-XXXXX	'1130	1130	TllD
l.TBD	TBD	BOC QC-XXXXX	TBD	TBD	TBD
1 mo	TBO	BQC QC . ,C.'YYY	TBD	TBD	TBD
4. TBD	TBO	BQC QC-XXXXX	1llD	IBO	TBD
). TBD	TBD	BQC QC-XXXXX	1130	llID	mo

EnteredBy: Date:

Reviewed By: Date:

Dispositim: PASSES sllbility ai XX-month time point

Comments: *N/A*= Not A 11cable

This procedure is made available throughfederal funds from the National Cancer Institute, NIH, under contract [redacted]

Attachment III

leidos

Leidos Biomedical Research, Inc.

MEMORANDUM

Date: iliiillllll

To: Biolo icalResources Branch DTP DCTD, NCI

Through: [redacted]
Manager, Biopharmaceutical Quality Assurance
BOP, Leidos Biomedical Research, Inc.

From: [redacted]
QualityControl
BOP, LeidosBiomedical Research,Inc.

Subject: Stability Results tor-.it 168-Months Final Vialed Product'

Enclosed is the Stability Results Report for at 168-Months, Final Vialed Product, Lot [redacted] This Lot of • • • was manufactured, filtered, vialed, and labeled by Leidos BiomedicaReseach, Inc. (formerl SAIC-Frederick, Inc.), for NCI-Frederick on September 23, 2003, as requested by BRB Program Director). This report is being sent to you at the request of in support of IND [redacted] Mayo Clinic. This report is being issued since the stability testing for the 168-month time point is complete

Testing for the 168-month stability time point for has met the required specifications as outlined in Stablity Protocol SP-101. Thereare no apparent trends leading to an out of specification result. The next stability time point will be at 180-months(September 2018).

Please reel free to contact me if you have any questions at [redacted] or e-mail at

Enclosures: Stability Results for [redacted] at 168-Months, Final Vialed Product, Lot [redacted]

pc: [redacted]

[redacted]

This procedure is made available through federalfunds from the National Cancer Institute, NIH, under contract [redacted]