



BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

TABLE OF CONTENTS

1. PURPOSE	1
2. SCOPE	1
3. RESPONSIBILITIES	2
4. PREPARATION OF ROOMS.....	2
5. PREPARATION OF PANS	2
6. PREPARATION OF VIALS.....	3
7. PREPARATION OF STOPPERS.....	5
8. PREPARATION OF CRIMPS/SEALS	6
9. SHELF-LIFE OF PREPARED VIALS, STOPPERS AND CRIMPS	8
10. DOCUMENTATION AND RECORDS.....	8
11. REFERENCES AND RELATED DOCUMENTS.....	9

1. PURPOSE

To describe the procedures for requesting, preparation, and sterilization of vials, stoppers, and crimps used in filling of final product.

2. SCOPE

The procedures in this SOP govern the requesting and preparation of container and closure components used in the filling of Current Good Manufacturing Practices (cGMP) final product by Biopharmaceutical Development Program (BDP) manufacturing personnel in the ATRF. This procedure applies both to manual and automated filling systems. Preparation of Biopharmaceutical Quality Assurance (BQA) released container and closure components will occur in Room [REDACTED]. The BDP uses Westar processed stoppers (pre-washed by West Pharmaceutical Services) as the main closure for glass vials. For components prepared in Room [REDACTED] sterilization will normally occur via a pass-through dry heat oven (OVEN-003-A) or clean steam autoclave (AUTO-005-A) into Room [REDACTED]. Sterilized components may be unloaded into Room [REDACTED] if filling is to be performed at a location other than the sterile core suite of rooms. Upon unloading the components from the sterilizer place them into a tertiary container that will maintain their cleanliness during transport. When using AUTO-011-A for sterilization, transport the material to be autoclaved to Room [REDACTED]. Unload sterilized components into Room [REDACTED] and place them into a tertiary container that will maintain their cleanliness during transport.



BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

Biopharmaceutical Quality Engineering (BQE) release of the utilized areas will be required for the facilities prior to work beginning.

3. RESPONSIBILITIES

- 3.1 Fill Finish Manager, Manufacturing, Biopharmaceutical Development Program (BDP)
- Defines this procedure.
 - Ensures BDP manufacturing personnel are trained in this procedure.
- 3.2 Manufacturing personnel
- Performs this procedure.
- 3.3 Biopharmaceutical Quality Assurance (BQA)
- Provides quality oversight.

4. PREPARATION OF ROOMS

- 4.1 Clean the Room(s) [REDACTED] and/or [REDACTED] as per **SOP 19408 - Cleaning and Disinfection of CGMP Areas in the ATRF.**
- 4.2 Stage all required components (vials, stoppers, crimps, etc.)
- 4.3 Verify that all items have been BQA released and are within their expiration date.
- 4.4 Ensure area and utilities are released for GMP processing as per **SOP 21554 – GMP Area Status Management.**

5. PREPARATION OF PANS

- 5.1 The parts washer will be operated according to **SOP 19411 – Operation and Maintenance of the Girton Parts Washer**, using the CIP 100/200 wash cycle.
- 5.2 Prior to vials being washed for a production run, vial pans will be washed in the Girton parts washer located in room [REDACTED]. The washing of the pans will be performed within a month before the vials are to be washed.
- 5.3 After the pans and lids are washed, the pan lids will be secured onto the pans so the pans are not open to the air in room [REDACTED]. Clean and secured vial pans will be labeled with the wash date and placed inside storage cage located in room [REDACTED] or MAL [REDACTED].

BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

6. PREPARATION OF VIALS

- 6.1 Obtain and complete Form 15105-01, when preparing vials.
- 6.2 Apply 1 BDP raw material release label from each lot of glass vials used to Form 15105-01.
- 6.3 Visually screen vials as they are removed from their packaging. Discard damaged, dirty, or otherwise unacceptable vials and document the number of vials rejected on Form 15105-01. Notify the Supervisor before proceeding if vials appear generally abnormal.
- 6.4 Wash vials per **SOP 15145 - Operation and Maintenance of the PennTech Vial Washer**.
- 6.5 Package glass vials for depyrogenation per the following instructions.
 - 6.5.1 Remove vials from washer and place upright in a clean stainless-steel pan obtained from the pan storage cart.
 - 6.5.2 Vials for closure integrity testing will be placed upright in the clean stainless-steel crimp check pan obtained from the pan storage cart.
 - 6.5.3 Dry the vials in the oven prior to depyrogenation. The lid will be securely placed onto the pan. The pans will be unwrapped at this time.
 - 6.5.3.1 Run the depyrogenation oven on the dry vials cycle per **SOP 15146 - Operation and Maintenance of the TPS Depyrogenation Oven**. Note on Form 15105-1 that the vials were dried.
 - 6.5.3.2 On completion of the drying cycle, remove pans from the oven.
 - 6.5.4 Wrap the pan with heavyweight oil free aluminum foil and seal with heat-resistant tape.
 - 6.5.5 A single wrapping of aluminum is required if the pan will be removed from oven into Room [REDACTED] for use in fill areas [REDACTED] or [REDACTED]. If the pan is removed in Room [REDACTED] for use in other fill areas, a double wrapping of aluminum foil will be required.

BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

- 6.6 Label the outside of each pan with the following information:
- 6.6.1 Vial BDP part number.
 - 6.6.2 Vial BDP lot number.
 - 6.6.3 Shelf life of processed vials (16 weeks from the sterilization date).
 - 6.6.4 Number of vials.
 - 6.6.5 Oven load number and run date.
 - 6.6.6 Initials and Date of the individual recording this information.
- 6.7 Vials for calibration, weight checks and will be packaged in groups of 10 vials and double wrapped with heavy duty oil-free aluminum foil. They will be placed on the top shelf of the oven.
- 6.8 Sterilize by dry heat sterilization using the depyrogenation cycle per **SOP 15146 - Operation and Maintenance of the TPS Depyrogenation Oven.**
- 6.9 Review the oven chart at the end of the cycle. Verify that the cycle ran according to oven load validation specifications. Sign and date the chart. A copy of the oven chart is required for cGMP BPR's.
- 6.10 If the oven did not perform properly, notify the Supervisor before proceeding.
- 6.11 Unload into Room [REDACTED] or [REDACTED].
- 6.11.1 Vials may be unloaded into Room [REDACTED] if filling is to be performed at a location other than the sterile core suite of rooms. Upon unloading the vials from the sterilizer place them in a tertiary container that will maintain their cleanliness during transport.
 - 6.11.2 Sterilized vials should be stored in Room [REDACTED] if not being used immediately.
 - 6.11.2.1 Vials for automated fills can be moved into the curtained area of Room [REDACTED] once the project cleaning of Room [REDACTED] is completed. Pans of vials moving into room [REDACTED] are sprayed with 70% IPA as they move into this ISO5 area.

BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

6.11.2.2 Vials for manual fills in the sterile core will be moved into Room [REDACTED] once the project cleaning of Room [REDACTED] is completed.

6.12 Complete Form 15015-01 for vial inspection, washing, and sterilization.

7. PREPARATION OF STOPPERS

7.1 Obtain and complete Form 15105-02, when preparing stoppers.

7.2 Stoppers should be free of dust and dirt upon receipt. If not, notify the Supervisor.

7.3 If necessary to repackage the needed number of stoppers from a larger bulk container, this should be done using sterile gloves and sleeve covers in a BSC. Take care to preserve the cleanliness and integrity of the remaining stoppers in the bulk container.

7.4 Westar stoppers are pre-washed and siliconized by the manufacturer. No further cleaning or treatment is necessary.

7.5 If the stoppers are not pre-cleaned at the manufacturer, wash and siliconize, the stoppers, if required as per **SOP 15103 - Operation of the DCI Washer Package Stoppers.**

7.5.1 Place approximately 1000 stoppers or less into an autoclave pouch, per Section 7.3. It may be necessary to divide the stoppers into more than one pouch depending on the quantity required. Place the stoppers into a second autoclave pouch. Pouches should be oriented in the autoclave to allow for steam penetration.

7.6 Label the outside of each pouch with the following information.

7.6.1 Stopper BDP part number.

7.6.2 Stopper BDP lot number.

7.6.3 Autoclave MEF #, run number and run date.

7.6.4 Shelf life of processed stoppers (16 weeks from the sterilization date).

7.6.5 Approximate number of stoppers.

7.6.6 Initials and Date of individual recording this information.

BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

- 7.7 Steam sterilizes the stoppers as per **SOP 19500 - Operation and Maintenance of the BMT Steam Sterilizers**.
- 7.8 Autoclaved stoppers may be unloaded into Room [REDACTED] if filling is to be performed at a location other than the sterile core suite of rooms. Upon unloading the stoppers from the sterilizer place them in a tertiary container that will maintain their cleanliness during transport. When using AUTO-011-A for sterilization, unloaded stoppers must be placed into a tertiary container that will maintain their cleanliness during transport.
- 7.9 Review the autoclave printout at the end of the cycle. Verify that the cycle ran according to the autoclave load validation specifications. Sign and date the printout. A copy of the autoclave printout is required for cGMP BPR's.
- 7.10 If the autoclave did not perform properly, notify the Supervisor before proceeding.
- 7.11 Unload the stoppers into Room [REDACTED], [REDACTED], or [REDACTED] (if autoclave AUTO-011-A is required).
- NOTE:** Stoppers may be unloaded into Room [REDACTED] or [REDACTED] if filling is to be performed at a location other than the sterile core suite. Upon unloading the stoppers from the sterilizer place them in a tertiary container that will maintain their cleanliness during transport.
- 7.12 Sterilized stoppers should be stored in Room [REDACTED] if not being used immediately. Stoppers for automated fills can be moved into the curtained area of Room [REDACTED] or [REDACTED] once the project cleaning of appropriate room is completed. Pouches of stoppers moving into room [REDACTED] are sprayed with 70% IPA as they move into the ISO5 area.
- 7.13 For preparation of Lyophilization stoppers only. Place the stoppers in double autoclaved pouches. After autoclaving, dry the stoppers in the depyrogenation oven per **SOP 15146 - Operation and Maintenance of the TPS Depyrogenation Oven**, using the stopper drying cycle to remove residual moisture from the stoppers. The autoclave bags must be positioned with the Tyvek side down.
- 7.14 Complete Form 15015-02 for stopper washing and sterilization.

8. PREPARATION OF CRIMPS/SEALS

- 8.1 Obtain and complete Form 15105-03, when preparing crimps.

BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

- 8.2 Visually screen the crimps/seals for cleanliness and for physical imperfections (bent crimps are most common). Discard any dirty or bent crimps.
- 8.3 Siliconize the crimps/seals if they will be used with the Flexicon filler as per **SOP 15121 - Siliconization of Aluminum Seals.**
- 8.3.1 To avoid storage of wet/damp aluminum seals, all seals will be dried immediately following siliconization.
- 8.3.2 If sterilized crimps/seals exceed their autoclave shelf life, they may be re-sterilized an additional time and then used within their new shelf life expiration date. The new expiration date of second sterilization will be added to the outside autoclave pouch with other identification listed in Section 8.5.
- NOTE:** Crimps/seals for manual fills do not require siliconization. If they exceed their autoclave expiration date they may be re-sterilized one time and used within their new expiration date. The new expiration date of second sterilization will be added to the outside autoclave pouch with other identification listed in Section 8.5.
- 8.4 Package the Crimp/Seals.
- 8.4.1 Place the crimps/seals approximately 1000 or less into an autoclave pouch. It may be necessary to divide the crimps/seals into more than one pouch depending on the quantity required.
- 8.4.2 Place a pouch of crimps/seals into a second pouch to sterilize. Pouches should be oriented as necessary to allow for steam penetration.
- 8.5 Label the outside of each pouch with the following information.
- 8.5.1 Crimp/seal BDP part number
- 8.5.2 Crimp/seal BDP lot number
- 8.5.3 Approximate number of crimps/seals
- 8.5.4 If siliconized, indicate Date of Siliconization
- 8.5.5 Autoclave MEF #, run number and run date
- 8.5.6 Shelf life of processed crimps/seals (16 weeks from the sterilization date)
- 8.5.7 Initials and Date of the operator recording this information.

BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

- 8.6 Steam sterilizes the crimp/seals as per **SOP 19500 - Operation and Maintenance of the BMT Steam Sterilizers.**
- 8.7 Autoclaved crimp/seals may be unloaded into Room [REDACTED] if filling is to be performed at a location other than the sterile core suite of rooms. Upon unloading the stoppers from the sterilizer place them in a tertiary container that will maintain their cleanliness during transport. When using AUTO-011-A for sterilization, unloaded stoppers must be placed into a tertiary container that will maintain their cleanliness during transport.
- 8.8 Review the autoclave on screen report and printout at the end of the cycle. Verify that the cycle ran according to specifications and is acceptable. Sign and date the printout. A copy of the autoclave printout is required for cGMP BPR's.
- 8.9 If the autoclave did not perform properly, notify the Supervisor before proceeding.
- 8.10 Unload the crimps/seals into Room [REDACTED], [REDACTED], or [REDACTED] (if autoclave AUTO-011-A is required).
- NOTE:** Crimps/seals may be unloaded into Room [REDACTED] or [REDACTED] if filling is to be performed at a location other than the sterile core suite. Upon unloading the crimps/seals from the sterilizer place them in a tertiary container that will maintain their cleanliness during transport.
- 8.11 Sterilized crimp/seals should be stored in Room [REDACTED] if not being used immediately. Crimp/seals for automated fills can be moved into the curtained area of Room [REDACTED] or [REDACTED] once the project cleaning of appropriate room is completed. Pouches of stoppers moving into room [REDACTED] are sprayed with 70% IPA as they move into the ISO5 area.
- 8.12 Complete Form 15015-02 for stopper washing and sterilization.

9. SHELF-LIFE OF PREPARED VIALS, STOPPERS, AND CRIMPS

- 9.1 The shelf-life of depyrogenated vials is sixteen (16) weeks from the depyrogenation oven run date based on current shelf life studies in PQ-115-E.
- 9.2 Stoppers or crimps/seals are given a shelf life of sixteen (16) weeks from the date of autoclaving, based on current shelf life studies in PQ-119.

10. DOCUMENTATION AND RECORDS

Completed copies of Forms 15105-01, 15105-02, and 15105-03 from this SOP are included with the BPR for the finished product.



BIOPHARMACEUTICAL DEVELOPMENT PROGRAM

SOP Title: Preparation of Vials, Stoppers, and Crimps for CGMP Filling of Final Product
SOP Number: 15105
Revision: 10

11. REFERENCES AND RELATED DOCUMENTS

Document Number	Title
15103	Operation of the DCI Washer
15121	Siliconization of Aluminum Seals
15145	Operation and Maintenance of the PennTech Vial Washer
15146	Operation and Maintenance of the TPS Depyrogenation Oven
19408	Cleaning and Disinfection of CGMP Areas in the ATRF
19411	Operation and Maintenance of the Girton Parts Washer
19500	Operation and Maintenance of the BMT Steam Sterilizers
21554	GMP Area Status Management
PQ-115-E	Shelf Life Stability for Wrapped Pans of Depyrogenated Vials
PQ-119	Shelf Life Stability for Stoppers and Crimps