Frede rick National Laboratory for
Cancer Research, Frederick, MD

BDP

Biopharmaceutica l Development Program

Standard Operating Procedure

Title: Preparing Reagent Solutions

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1.0 Purpose

This procedure defines a method for preparing Reagent Solutions according to Current Good Manufacturing Practices (CGMPs).

2.0 Scope

This SOP governs the preparation of reagent solutions produced in the Biopharmaceutical Development Program (BOP), by trained manufacturing personnel, for use in CGMP, Research and Development, and stock solution applications. It defines the criteria for obtaining area clearance, acceptance of raw materials, formulation procedures, documentation, storage and

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final release of each reagent solution. This SOP does not apply to the preparation of solutions intended to be shipped directly to clinical sites for use as diluents for products that will be administered to humans. Such diluents are considered CGMP products and are manufactured following a preapproved Master Production Record (MPR) and area clearance specific to the product.

NOTE: Some solutions that are prepared concurrently with upstream processing are governed by and recorded directly into the production batch record. Those reagent solutions are not governed by this SOP.

3.0 Authority and Responsibility

3.1 The Director, Technical Operations, has the authority to define this procedure.

3.2 The Manager of Manufacturing Support Services, or designee, (a designee is someone other than a preparer of the buffer or solution) is responsible for training personnel in this procedure and for providing documentation of training to Biopharmaceutical Quality Assurance (BQA).

3.3 BDP personnel are responsible for implementation of this procedure.

3.4 Process Analytics\Quality Control (PA\QC) is responsible for performing tests on high-risk buffers and submitting the results of the testing to BQA.

3.5 BQA is responsible for quality oversight of this operation.

4.0 Rationale

4.1 The procedures described in this document are intended to provide the controls necessary to ensure the manufacture of reagent solutions according to CGMP standards. The preparation of reagent solutions not requiring a CGMP level of control (e.g., some research and development materials, etc.) may not need to follow these procedures and could be produced according to a different set of requirements. Those requirements would be determined jointly by the requester and the Manager of Manufacturing Support Services.

4.2 A wide variety of reagent solutions are produced which in turn find their use in various stages of the development and purification process. Categories have been established that match appropriate release testing and document review for each reagent solution (buffer) based on potential impact to the finished product. The categories are as follows.

4.3 The preparation of reagent solutions and buffers is documented on data capture forms as specified in ***SOP 15107 - Request for Reagent Solutions***.

4.4 Low Risk Buffers (BPR-R-06 & BPR-R-08)

- Sanitants used for cleaning and storage of columns and resins, etc. (sodium hydroxides, ethanol, 6M Guanidine HCl).
- Stock Solutions (acids and bases used for pH adjustment).

4.5 Moderate Risk Buffers (BPR-R-07)

- Would include a wide variety of “In-Process” solutions that are not used as final formulation buffers.

4.6 High Risk Buffers (BPR-R-04)

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- All final formulation buffers and any other buffers determined by the Project Scientist to have potential for serious impact on the quality of the finished product.

4.7 R&D Buffers (BPR-R-05)

- Buffers used in R&D

4.8 Buffer for Toxicology Studies (BPR-R-09)

- Solutions that will be used in Toxicology Studies as diluents or Negative Controls.
- Buffers will be released on COA by BQA.

5.0 Materials, Equipment, and Environmental Requirements

5.1 Chemicals

5.1.1 Only BDP part numbers as specified on the Batch Production Record are to be used as per ***SOP 15107 - Request for Reagent Solutions***.

5.1.2 Chemical containers must have green "released" stickers attached. Clearance of chemicals is controlled by BQA as defined in ***SOP 21903 - Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications.***

NOTE: Chemicals may be received for R&D purposes that are labeled with a blue and white "For R&D Use Only" sticker. R&D chemicals must not be antibiotics, toxins, or of protein origin. Chemical grades of R&D chemicals must be comparable to those released for GMP production.

5.1.3 Chemicals must be within the expiration date as indicated on the release label.

5.2 WFI

5.2.1 Prepare reagent solutions using WFI Quality Water.

NOTE: WFI from the in-house system must be drawn within 24 hours of use. WFI sterile filtered into a sterile container has a one-year expiration date.

5.2.2 WFI from an outside vendor must be released for use by BQA according to ***SOP 21903 - Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications***

5.3 Filters

5.3.1 The BDP Part Number and R number for the filter used for a specific production will be recorded in the Batch Production Record (BPR).

5.3.2 Filters must be within their expiration date as indicated on the release label.

5.4 Containers and Closures

5.4.1 Containers and closures used are recorded in the BPR.

5.4.2 Containers and closures must be within their expiration date as indicated on the release label.

5.5 Reusable Equipment (Product Contact)

5.5.1 Reusable equipment for the preparation of reagent solutions includes, but is not limited to, the following.

5.5.1.1 Mixing/stirring equipment (e.g., stainless steel shafts and propellers, Teflon stir bars, etc.).

5.5.1.2 Assorted glass and plasticware (e.g., beakers, volumetric flasks, large scoops, graduated cylinders, etc.).

5.5.2 Reusable equipment will be immediately rinsed with WFI following use and then double-rinsed with hot WFI. If non water-soluble items such as lipids, or components where carryover would present potential risk, it is recommended to use disposable equipment as additional cleaning using detergent may otherwise be required. Items may be autoclaved to reduce bioburden on non-sterile process equipment before use. Visually inspect for cleanliness before autoclaving or before use.

5.6 Disposable Equipment (Product Contact)

5.6.1 Disposable equipment for the preparation of reagent solutions includes, but is not limited to:

- Pre-sterilized plastic tank liners.
- Pre-sterilized pipets.
- Pre-sterilized filter units.
- Silicone tubing.
- Pre-sterilized syringe and needle.
- Weigh boats.
- Sampling spoons and scoops.

5.6.2 Disposable items are intended for single use and must be discarded after preparation of the solution.

5.7 Top-Loading and Analytical Balances

NOTE: Top-loading and analytical balances are intended for use in the weighing of chemicals and for density determinations. A weighed quantity > 400 grams will be rounded to one (1) decimal place (use a balance with readability to 1-tenth of a gram) and a weighed quantity < 400 grams will be rounded to two (2) decimal (use a balance with readability to one hundredth of a gram) or two significant digits to the right of the decimal. (Use a balance of acceptable readability.) Detailed procedures on the use and operation of a balance can be found in ***SOP 21500 - General Policies and Procedures for Balances***.

5.7.1 Verify that the balance is level and within its calibration period.

5.7.2 Check the balance on the day of use against standard weights before use as per the appropriate SOP indicated above.

5.8 Floor Scales

NOTE: Floor scales are intended for use in determining and recording the volume of liquid in the mixing vessel and to determine and record fill volumes of finished product dispensed into flexible packaging.

5.8.1 Verify that the scale is within its calibration period.

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5.8.2 Sartorius Floor Scale, ISI-30 Indicator, BDP equipment number 73590 is used for weighing 20 KG - 600 Kg.

5.8.3 Mettler Floor Scale BDP equipment number BALN-001-A, is used for weighing 10 Kg – 1300 Kg

5.9 pH Meter

5.9.1 The use of pH meters is described in ***SOP 12181 - Measurement of pH Using a pH Meter.***

5.9.2 The pH meter must be standardized each day before use for the appropriate range.

5.10 Conductivity Meter

5.10.1 The use of the conductivity meter is described in ***SOP 15133 - Operation of the Orion Conductivity Meter, Model 150 USP***.

5.10.2 The conductivity meter must be standardized each day before use for the appropriate range.

5.11 Laminar Flow Biological Safety Cabinet

5.11.1 When performing aseptic filling operations (including the processing of Process Analytics [PA] samples) inside a Laminar Flow Biological Safety Cabinet (BSC), the following steps must be followed.

5.11.1.1 Verify that the BSC is within its certification period.

5.11.1.2 Operators must put on sterile gloves and sterile sleeves.

5.11.1.3 Disinfect the hood as per ***SOP 19102 - Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers, and Centrifuges*** prior to and after use.

5.11.1.4 Disinfect items to be brought into the hood with 70% Isopropyl alcohol.

5.11.1.5 Record each activity on the Biological Safety Cabinet Use, Maintenance, Disinfection, and Calibration Logsheet (Form 19102-02).

5.12 Environment/Personnel

5.12.1 The weighing of chemicals, mixing and dispensing operation will occur in approved areas.

NOTE: Clearance of the area by BQA as per ***SOP 21554 - GMP Area Status Management*** is required prior to production of CGMP reagent solutions. For proper gowning for personnel during reagent preparation, reference ***SOP 19406 - Gowning Requirements for Personnel and Visitors: [redacted] Manufacturing and Support Areas***.

5.12.2 Only one product will be worked on at a time in order to avoid mix-ups and potential for cross-contamination. The room in use will be cleared of clutter. Unneeded materials will be stored properly prior to beginning work.

5.12.3 During production, access to the area will be limited to personnel directly involved with the process and BQA auditors or other regulatory inspectors, if necessary.

5.12.4 Cleaning of Room A2429 is performed as per ***SOP 19408 - Cleaning and Disinfection of CGMP Areas in the*** [redacted].

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6.0 Formulation of Reagent Solution

NOTE: The preparation of a reagent solution is done following the requirements specified in the Batch Production Record in accordance with CGMP guidelines. The technician must fill in all required information as requested paying particular attention to the following.

6.1 Standardize the following equipment prior to use.

6.1.1 pH meter.

6.1.2 Conductivity meter.

6.1.3 Balances used for weighing chemicals.

6.2 Measure out required amounts of components as specified in the chemistry formulation.

6.2.1 Include, where applicable, a printout from each balance used. Include the following information on the printout and tape it to the chemistry formulation worksheet when completed.

- Tare.
- Weight of component (multiple weighings of the same component must be separated by a tare weight).
- Date, BDP component part number, and signature of operator.

6.2.2 Only one chemical component can be open at a time in order to avoid cross-contamination.

6.2.3 The weigh out of a chemical must be witnessed by a second individual.

6.3 Prepare Mixing Vessel

Option #1 (When determining volume by weight)

6.3.1 Zero floor scale.

6.3.2 Place appropriate size container on floor scale.

6.3.3 Insert pre-sterilized tank liner.

6.3.4 Set up mixing/stirring equipment of appropriate size for the batch to be formulated.

6.3.5 Tare scale and print.

Option #2 (When determining volume using calibration marks)

6.3.6 Choose the appropriate size mixing vessel.

6.3.7 Insert pre-sterilized tank liner.

NOTE: A tank liner will not be required for batch sizes ≤ 20L.

6.3.8 Set up mixing/stirring equipment of appropriate size for the batch to be formulated.

6.4 Add Components

6.4.1 Add required quantity of WFI as per the batch production record. Print weight when using floor scale.

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6.4.2 Turn on the mixer/stirrer and adjust speed to create adequate conditions for obtaining solubility of components. See the note in Section 6.4.4.

6.4.2.1 Mixing/stirring is continuous throughout the entire formulation process, i.e., following initial addition of WFI through addition of components and pH adjustment. Final Quantity Sufficient (Q.S.) is performed with the mixer turned off.

6.4.2.2 Record total mixing/stirring time in the chemistry formulation section of the BPR.

6.4.3 Add required quantities of chemicals in the order specified. The addition of components to the batch must be witnessed by a second individual.

6.4.4 Components must be completely in solution before proceeding.

NOTE: When no undissolved material is detected by visual observation, continue to stir for an additional 5 minutes.

6.5 Adjust pH as required.

NOTE: Unless otherwise stated, the final pH will be determined for a sample at 25ºC.

6.5.1 Adjustments will be made as per the instructions. Allow a minimum of one minute of additional mixing time prior to rechecking the pH value.

6.5.2 The addition of acids and bases to adjust pH must be made with extreme care to avoid overshooting the specification.

NOTE: Having to correct the pH due to overshooting the specified range can have adverse effects on the solutions conductivity and may result in failure to pass product release testing and/or to perform properly.

6.6 Q.S. to Final Volume

NOTE: Steps 6.6.1 through 6.6.4 apply when using the floor scale.

6.6.1 Bring solution to within 5% of final volume.

6.6.2 If the specific gravity is not listed in the BPR, determine the specific gravity by measuring the weight of a known volume on a standardized balance.

6.6.3 Convert the final volume required from liters to kilograms.

6.6.4 Fill to the final volume in kilograms and print weight.

6.6.5 Mix for a minimum of five minutes.

6.7 Measure conductivity and record if required.

7.0 Filtration of Product

7.1 For sterile product, a 0.2-micron, sterilizing grade filter is required. Additional requirements for filtration may be specified by the Project Scientist when requesting the reagent solution.

7.2 Make all aseptic connections inside the Laminar Flow Hood.

7.2.1 Wipe down hood surfaces with disinfectant prior to the start of a run as per ***SOP 19102 - Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers, and Centrifuges***.

7.2.2 Operators must disinfect their gloves with 70% IPA before entering the hood.

NOTE: The filter (if not supplied sterile) and any tubing, etc., attached to the downstream side of the filter must be prepared and sterilized as per ***SOP 15126 - Preparation of Supplies for Autoclave Sterilization***. Good aseptic technique is critical when making connections downstream of the filter to ensure the sterility of the finished product.

7.3 Filling operations that expose product downstream from the filter to the atmosphere must occur inside the Laminar Flow Hood.

7.4 The filter must be integrity tested post-use.

7.4.1 Flush with WFI following use. In some cases, it may be necessary to pre-soak with alcohol to remove surfactants, etc., from the filter prior to performing the integrity test.

7.4.2 If more than one filter is used before the filter is integrity tested, the filter will be labeled with product Part Number and Lot Number and other information as necessary to distinguish between filters.

7.4.3 Integrity test the filter as per ***SOP 15114 - Bubble Point Test for 0.2 Micron Filters*** or ***SOP 12197 - Testing Filters with the Palltronic Flowstar Integrity Test System.*** Integrity test specifications are as per the manufacturer. Record the equipment information (MEF #, Calibration due date, etc.) and method used for testing in the BPR.

NOTE: If the filter fails to meet the manufacturer's specifications for integrity test, reflush the filter and repeat the test. If the filter continues to fail the integrity test, retain the filter for the filter failure investigation. If the retest fails, the product must be refiltered with a new filter or discarded.

8.0 Final Solution Filling, Labeling, and Preparation of QC Samples

8.1 Place all supplies inside the hood prior to filling.

NOTE: This is best accomplished with two people. One person disinfects the material with 70% IPA or opens the outer wrap of pre-sterilized materials while the other person operates within the hood, touching only sterile or disinfected materials.

8.2 Print the buffer labels as specified in the production record.

8.2.1 A second operator must approve the buffer labels prior to use.

8.2.2 Buffer label accountability is included in the Batch Production Record.

8.3 Filling of Bottles

8.3.1 Filter apparatus can provide for a filling bell that is suspended over the mouth of the bottle. A peristaltic pump is used to transfer liquid from the mixing vessel, through the filter, and into the bottle.

8.3.2 Remove the cap from the bottle and fill the bottle to the appropriate volume as specified in the Batch Production Record.

- Fill PA\QC samples as required for testing. PA\QC samples are taken as close to the beginning of the filling operation as possible.

- For high-risk buffers, samples are submitted to PA\QC along with Form 22002-01 (Quality Control Test Request) and a copy of the product release specifications. A copy of the Test Request is attached to the Batch Production Record after a PA\QC number is assigned.

8.3.3 Tighten the cap on the bottle and pass the bottle out of the hood.

8.3.4 Apply the product label squarely on the bottle along with a PA\QC quarantine label. Quarantine labels are not required for R&D, Stock Solutions preparations or Final Product for External Clients (BPR-R-09).

8.3.5 Store the bottles as specified on the label.

8.4 Aseptic Filling of Bags

8.4.1 A section of pre-sterilized tubing with the appropriate Colder™ fitting is used to aseptically connect the filter to each bag for filling. A peristaltic pump is used to transfer liquid from the mixing vessel, through the filter, and into the bag.

8.4.2 Remove the nipple cover from the inlet port of the bag and aseptically connect the tubing from the filter. Make sure all clamps on the inlet path to the bag are open.

8.4.3 Close the clamp on the outlet port of the bag.

8.4.4 Fill the bag to volume as specified in the Batch Production Record.

NOTE: Follow Steps 8.4.4.1 through 8.4.4.2 when using the floor scale.

8.4.4.1 Tare the floor scale and print.

8.4.4.2 Fill the bag to the specified volume by weight using the floor scale to read the amount dispensed in kilograms (a conversion from liters to grams is necessary using the density as determined during formulation). Print the weight indicated on the floor scale after filling is completed for each bag.

8.4.5 Aseptically fill the PA\QC samples for high-risk products as required for testing. PA samples are taken at the end of the filling operation.

8.4.5.1 Samples are submitted to PA\QC along with Form 22002-01 and a copy of the release specifications. A copy of the Test Request is attached to the Batch Production Record after a PA\QC number is assigned.

8.4.6 Clamp off the tubing upstream of the Colder™ fitting and drain the liquid from tubing into the bag. Close the clamp on the inlet port of the bag. Disconnect the bag and apply a sterile sealing cap to the inlet port. Reconnect the tubing to a new bag and repeat the process until all bags have been filled.

8.4.7 Cable-tie the clamps to keep closed.

8.4.8 Apply the product label to each bag along with a quarantine label. Quarantine labels are not required for R&D, Stock Solutions and Final Product for External Clients.

8.5 Reagent and Solution Storage

8.5.1 Store as specified on the label.

8.5.2 Quarantine solutions are to be stored in [redacted] until released and must be physically segregated with signage clearly indicating

quarantine status. Quarantine material may be staged in other production areas with approval from BQA.

8.5.3 Quarantined reagent solutions should not be stored in any manufacturing corridors or manufacturing suites.

8.5.4 Released reagent solutions should not be stored in corridors in such a manner that would impede entry or exit into any area or violate fire code.

9.0 Review and Approval

NOTE: The following requirements for release testing and document review are listed for each of the categories of reagent solutions (buffers) as described in the Rationale Section.

9.1 Low Risk Buffers (stock solution produced using BPR-R-06)

9.1.1 The operators review the Batch Production Record for completeness and accuracy.

9.1.2 Stock solution may be used immediately for production.

9.1.3 The Batch Production Record is then delivered to the Manager of Manufacturing Support Services who will adjust the chemical inventory.

9.1.3.1 Record quantities of chemicals used on the Component Inventory Cards (see Attachment 1). A disposition for each chemical component used must be indicated on the card for accountability.

9.1.3.2 For reagent solutions, this includes the part and lot number of the finished product.

9.1.4 The Manager, or designee, of Manufacturing Support Services will perform a final review of the Batch Production Record including manufacturing test results as required. The document will be forwarded to BQA for review.

9.1.5 BPRs will be given to BQA for review.

9.1.6 Upon completion of BQA review, the document will be scanned by BQA into an electronic file named "Chemist Batch Records (scanned)" [redacted]. The original is entered only in the BQA [redacted].

NOTE: The electronic file will be a PDF format and will be "Read-Only" for BOP Manufacturing, BQA Auditing, and Regulatory Affairs personnel.

9.2 Low Risk Buffers: Cleaning Solutions (BPR-R-08) and R&D Buffers (BPR-R-05)

9.2.1 The operators review the Batch Production Record for completeness and accuracy.

9.2.2 The Batch Production Record is then delivered to the Manager, or designee, of Manufacturing Support Services, for Adjustment of Chemical Inventory.

9.2.2.1 Record quantities of chemicals used on the Component Inventory Cards (see Attachment 1). A disposition for each chemical component used must be indicated on the card for accountability.

9.2.2.2 For reagent solutions, this includes the part and lot number of the finished product.

9.2.3 The Manager, or designee, of Manufacturing Support Services will perform a final review of the Batch Production Record including manufactuirng test results as required.

9.2.3.1 Manufacturing test results must meet release specifications established in the BPR.

9.2.4 The Manager of Manufacturing Support Services will approve the BPR and prepare release stickers.

9.2.5 Manufacturing personnel apply release stickers to each product container. A copy of the release stickers will be attached to the BPR, and the BPR will be signed and dated indicating the release of the buffer was completed.

9.2.5.1 CGMP reagent solutions will receive green release stickers.

9.2.5.2 R&D reagent solutions will receive blue and white release stickers indicating "FOR R&D USE ONLY."

9.2.6 BPRs for GLP or CGMP solutions will be given to BQA for review.

9.2.7 Upon completion of BQA review of the GLP or CGMP solutions, the document will be scanned by BQA into an electronic file named "Chemist Batch Records (scanned)" located at: [redacted]
The original is then filed by BQA in the BQA [redacted].

9.2.8 BPRs for R&D Solutions will be maintained by Manufacturing and filed in the office of the manufacturing manager. After five years, they are archived with BQA.

9.3 Moderate Risk Buffers: In-Process (BPR-R-07)

9.3.1 The operators review the Batch Production Record for completeness and accuracy.

9.3.2 The Batch Production Record is then delivered to the Manager, or designee, of Manufacturing Support Services, for Adjustment of Chemical Inventory.

9.3.2.1 Record quantities of chemicals used on the Component Inventory Cards (see Attachment 1). A disposition for each chemical component used must be indicated on the card for accountability.

9.3.2.2 For reagent solutions, this includes the part and lot number of the finished product.

9.3.3 The Manager, or designee, of Manufacturing Support Services will perform a final review of the Batch Production Record including manufactuirng test results as required.

9.3.3.1 Manufactuirng test results must meet release specifications established in the BPR.

9.3.4 The Manager or designee of Manufacturing Support Services, will approve the BPR and prepare release stickers.

9.3.5 Manufacturing personnel apply release stickers to each product container. A copy of the release stickers will be attached to the BPR and the BPR will be signed and dated indicating the release of the buffer was completed.

9.3.5.1 CGMP reagent solutions will receive green release stickers.

9.3.6 BPRs for GLP or CGMP Solutions will be given to BQA for review.

9.3.7 Upon completion of BQA review, the document will be c [redacted] BQA into an [redacted] electronic file named "Chemist [redacted] Batch Records (scanned)" [redacted]. The origina ls en i e y in the BQA [redacted].

9.4 High Risk Buffers (BPR-R-04)

9.4.1 The operators review the Batch Production Record for completeness and accuracy.

9.4.2 The Batch Production Record is then delivered to the Manager, or designee, of Manufacturing Support Services, for Adjustment of Chemical Inventory.

9.4.2.1 Record quantities of chemicals used on the Component Inventory Cards (see Attachment 1). A disposition for each chemical component used must be indicated on the card for accountability.

9.4.2.2 For reagent solutions, this includes the part and lot number of the finished product.

9.4.3 The Manager, or designee, of Manufacturing Support Services will perform a final review of the Batch Production Record including manufacturing test results as required.

9.4.3.1 Manufactuirng test results must meet release specifications established in the BPR.

9.4.3.2 The Manager or designee, of Manufacturing Support Services, will approve the BPR and will give the BPR to BQA for review.

9.4.4 A final review of the Batch Production Record and any PA test results will be performed by BQA. Once approved for release, BQA returns the BPR to Manufacturing Support Services for the labeling of the containers with Release stickers.

9.4.5 The Manager or designee, of Manufacturing Support Services will prepare release stickers.

9.4.6 Manufacturing personnel apply release stickers to each product container. A sample of the release stickers will be attached to the BPR and the BPR will be signed and dated indicating the release of the buffer was completed.

9.4.7 Manufacturing returns the BPR to BQA. BQA checks that the documentation of the product is complete. The document will be scanned b BQA into an electronic file named "Chemist [redacted] Batch Records (scanned)" [redacted] The original is then filed by BQA in the BQA [redacted].

9.5 Buffers for Tox Studies (BPR-R-09)

9.5.1 The operators review the Batch Production Record for completeness and accuracy.

9.5.2 The Batch Production Record is then delivered to the Manager, or designee, of Manufacturing Support Services, for Adjustment of Chemical Inventory.

9.5.2.1 Record quantities of chemicals used on the Component Inventory Cards (see Attachment 1). A disposition for each chemical component used must be indicated on the card for accountability.

9.5.2.2 For reagent solutions, this includes the part and lot number of the finished product.

9.5.3 The Manager, or designee, of Manufacturing Support Services, will perform a final review of the Batch Production Record including manufacturing test results as required.

9.5.3.1 Manufacturing test results must meet release specifications established in the BPR.

9.5.3.2 The Manager or designee, of Manufacturing Support Services, will approve the BPR and will give the BPR to BQA for review.

9.5.4 On completion of requested testing, Process Analytics\Quality Control will generate a COA.

9.5.5 A final review and approval of the Batch Production Record and COA will be performed by BQA.

9.5.6 U on com letion of BQA review, the document will be scanned by BQA into the appropriate project file [redacted] The original is then filed by BQA in the BQA [redacted].

10.0 References and Related Documents

10.1	**SOP 12181**	*Measurement of pH Using a pH Meter*
10.2	**SOP 12197**	*Testing Filters with the Palltronic Flowstar Integrity Test* System
10.3	**SOP 15107**	*Request for Reagent Solutions*
10.4	**SOP 15114**	*Bubble Point Test for 0.2 Micron Filters*
10.5	**SOP 15126**	*Preparation of Supplies for Autoclave Sterilization*
10.6	**SOP 15133**	*Operation of the Orion Conductivity Meter, Model 150 USP*
10.7	**SOP 19102**	*Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers, and Centrifuges*
10.8	**SOP 19406**	*Gowning Requirements for Personnel and Visitors: - Manufacturing and Support Areas*
10.9	**SOP 19408**	*Cleaning and Disinfection of CGMP Areas in the-*
10.10	**SOP 21500**	*General Policies and Procedures for Balances*
10.11	**SOP 21554**	*GMP Area Status Management*
10.12	**SOP 21903**	*Using the Part Number/Master Specification Program to Establish Raw Material Part Numbers and Master Specifications*

11.0 Attachments

11.1 Attachment 1 Form 15100-01, Component Inventory Card

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Attachment 1

Form 15100-01, Component Inventory Card

FNLCR, BDP
Form No.: 15100-01
SOP No.: 15100
Revision 10: APR 08 2019

Component Inventory Card

Material: _____ R #: _____

BDP #: _____ Exp. Date: _____

Date	Units Removed	Disposition	Performed By

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