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2.3.P PLACEBO (PLACEBO FOR INJECTION)

2.3.P.1 DESCRIPTION AND COMPOSITION OF PLACEBO FOR INJECTION

The placebo is provided as a sterile, preservative-free, lyophilized powder in an 8 mL, Type I glass vial. A vial of placebo includes the excipients Mannitol USP, Sucrose NF, and Tromethamine USP. During compounding 1 N Hydrochloric Acid is added to adjust the pH of the formulation buffer. The lyophilized placebo is reconstituted with either 1 mL of Sterile Water for Injection USP (SWFI) or 1 mL of Bacteriostatic Water for Injection USP (BWFI) administration. After reconstitution the volume of the placebo is approximately 1.05 mL.

2.3.P.1.1 Composition (Placebo for Injection)

The quantitative formulation of the placebo is presented in [Table 1](#).

Table 1: Unit Formula of Placebo

| Ingredients | Quantity per vial | Quantity per mL | Pharmaceutical Function | Quality Standards |
|-----------------------------|-------------------|-----------------|-------------------------|-------------------|
| Inactive Ingredients | | | | |
| Mannitol | 42.0 mg | 40.0 mg | Bulking agent | USP |
| Sucrose | 10.5 mg | 10.0 mg | Stabilizer | NF |
| Tromethamine | 1.27 mg | 1.21 mg | Buffer component | USP |
| 1 N Hydrochloric Acid | q.s. ¹ | NA | pH adjustment | Footnote 2 |
| Water for Injection | NA ³ | 1 mL | Solvent | USP |
| Nitrogen | q.s. ⁴ | NA | Vacuum neutralization | NF |

q.s. = Quantity sufficient; NA = Not applicable

¹ Quantity sufficient to adjust the pH to 7.2 – 7.6.

² For adjusting the pH, a 1 N Hydrochloric Acid solution is prepared with Hydrochloric Acid NF and Water for Injection USP.

³ The water is essentially removed during lyophilization.

⁴ The vials are backfilled with nitrogen prior to complete stopper insertion.

2.3.P.2 PHARMACEUTICAL DEVELOPMENT

Not applicable.

2.3.P.3 MANUFACTURE

2.3.P.3.1 Manufacturers

Placebo for Injection manufacturing, primary and secondary packaging (with labeling to identify as placebo) are performed in accordance with current Good Manufacturing Practices at the following facility:

Patheon Manufacturing Services LLC (Patheon)
5900 Martin Luther King Jr. Highway
Greenville, NC 27834
United States

FDA Facility Establishment Identifier (FEI): 1018495
Data Universal Numbering System (DUNS): 079415560

Placebo for Injection storage, primary and secondary labeling, and assembly, QP release and distribution are performed in accordance with current Good Manufacturing Practices at the following facility:

Victoria Pharmaceuticals
The Plenum Building
Royal Group of Hospitals Site
Grosvenor Road
Belfast BT12 6BA
United Kingdom

MHRA Site Number: 1683129
MIA (IMP) Number: 32485

Placebo for Injection is imported by:

Tanner Pharma UK Limited
The Tithe Barn
Harpendenbury Farm, Harpendenbury
Redbourn, St. Albans AL13 7QA
United Kingdom

Release and stability testing of Placebo for Injection are performed at the following facilities:

Table 2: Testing Facilities and Tests Performed

| Testing Facility | Release Testing | Stability Testing |
|---|---|--|
| Partner Therapeutics, Inc. 2625 162 nd Street SW Lynnwood, WA 98087 United States FDA FEI: 3007934434 DUNS: 081059614 | All tests except for USP <790>, bacterial endotoxins, sterility, and particulate matter | All tests except for particulate matter. |
| Patheon Manufacturing Services LLC 5900 Martin Luther King Jr. Highway Greenville, NC 27834 United States | USP <790>, bacterial endotoxins, and sterility | Not Applicable |

| Testing Facility | Release Testing | Stability Testing |
|---|--------------------|--------------------|
| Nitto Avecia Pharma Services, Inc. 10 Vanderbilt Irvine, CA 92618 United States FDA FEI: 3012971227 DUNS:116975565 | Particulate matter | Particulate matter |

2.3.P.3.2 Batch Formula

The batch formula for the manufacture of Placebo for Injection is provided in [Table 3](#). The batch formula will be used as stated. The actual quantity of excipients used may differ based on reasonable variation of target value (i.e., cumulative variation not more than $\pm 10\%$).

Table 3: Batch Formula of the Placebo for Injection

| Ingredient | Reference to Standards | Per Liter Quantity ¹ |
|-----------------------|------------------------|-------------------------------------|
| Mannitol | USP | 42 g |
| Sucrose | NF | 10.5 g |
| Tromethamine | USP | 1.21 g |
| 1 N Hydrochloric Acid | Footnote 4 | q.s. ⁵ |
| Water for Injection | USP | q.s. to 1 kg (approximately 0.98 L) |
| Nitrogen ⁶ | NF | q.s. |

q.s. = Quantity sufficient

¹ Actual quantities of excipients dispensed may vary slightly from the theoretical batch formula (i.e., cumulative variation not more than $\pm 10\%$).

² A volume of 58 liters is compounded to manufacture approximately 54,000 vials that includes approximately 4 liters for filter flushes.

³ Also referred to as tris(hydroxymethyl)aminomethane (i.e., TRIS).

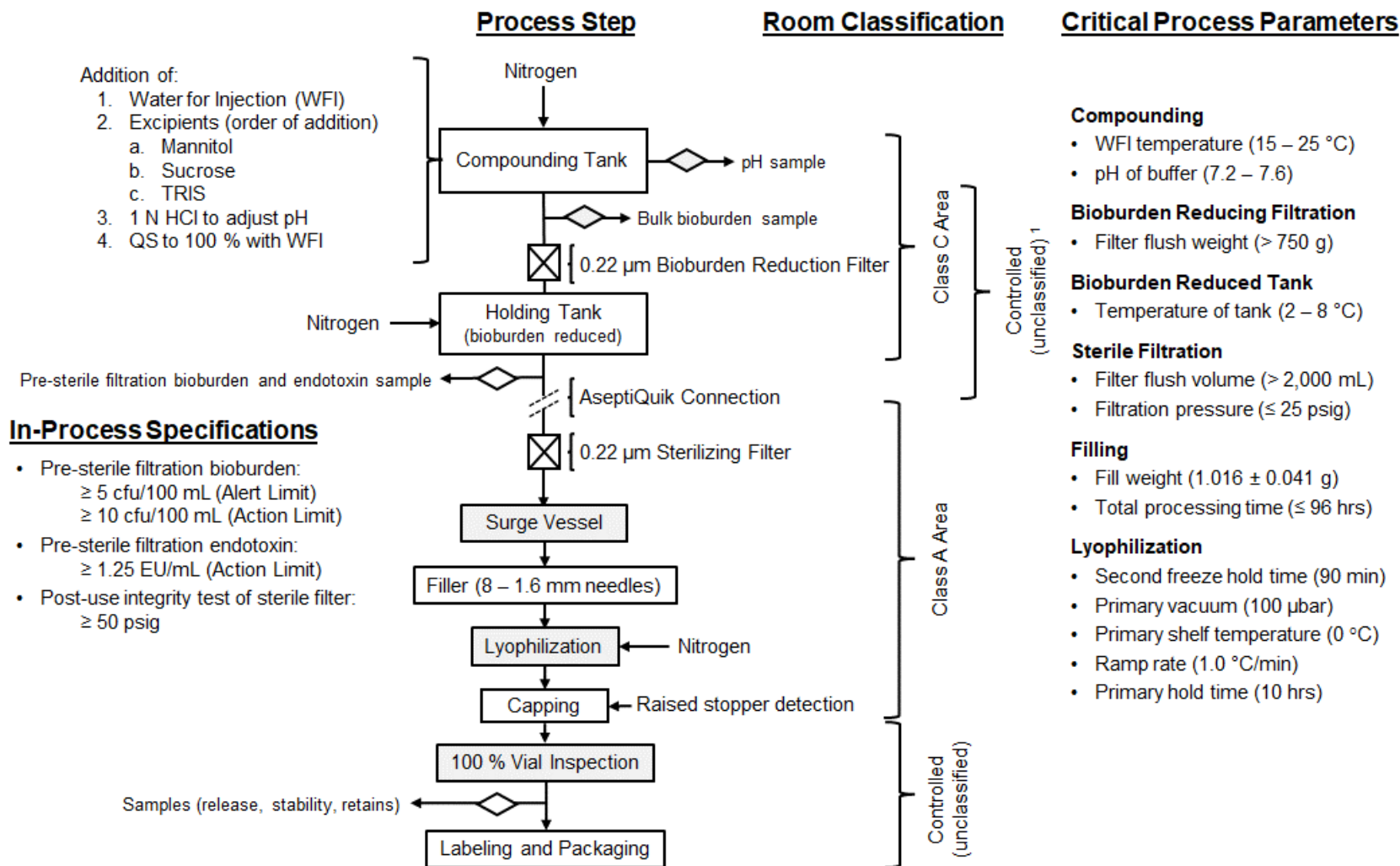
⁴ For adjusting the pH, a 1 N Hydrochloric Acid solution is prepared with Hydrochloric Acid NF and Water for Injection USP.

⁵ Quantity sufficient to adjust pH 7.2 – 7.6.

⁶ The vials are backfilled with nitrogen to neutralize the vacuum of the lyophilization step prior to stopper insertion.

2.3.P.3.3 Description of Manufacturing Process and Process Controls

A schematic of the manufacturing process, including critical process parameters (CPPs), is provided in [Figure 1](#).

Figure 1: Schematic of the Placebo Manufacturing Process

2.3.P.3.3.1 Compounding

In a Class C area, a dedicated stainless-steel 120-liter compounding tank is placed on a floor scale and $80\% \pm 0.2$ kg of the calculated amount of Water for Injection (WFI) at $15 - 25\text{ }^{\circ}\text{C}$ is added to the tank. The quantity of excipients Mannitol USP, Sucrose NF, and Tromethamine USP are calculated on a per L basis for the intended batch.

Mannitol, sucrose, and TRIS (tromethamine) are added individually to the compounding tank in the order presented. After each addition the solution is mixed (200 ± 10 rpm) and dissolution is confirmed by visual observation. With mixing (200 ± 10 rpm) 1 N HCl is added to the compounding tank to adjust the pH of the bulk placebo buffer to $7.2 - 7.6$. The solution is mixed, the tank is sampled, and the pH measured. If the pH is not within range, incremental amounts of 1 N HCl are added to the bulk solution. After each addition of 1 N HCl the tank is mixed (200 ± 10 rpm) prior to measuring the pH.

WFI ($15 - 25\text{ }^{\circ}\text{C}$) is added to the placebo solution to the batch weight (± 0.2 kg). After WFI addition is complete, the solution is mixed at 200 ± 10 rpm. The maximum allowed time from start of filling the tank with WFI to the bioburden reduction filtration process step is ≤ 24 hr.

2.3.P.3.3.2 Bioburden Reduction Filtration

The compounding tank is connected to a $0.22\text{ }\mu\text{m}$ hydrophilic cartridge filter which leads to a holding tank. Using filtered nitrogen, the compounding tank is pressurized to 27.5 psia, the bottom valve opened, and the placebo solution filtered into the holding tank. A bubble point integrity test is performed on the $0.22\text{ }\mu\text{m}$ filter pre- and post-filtration. To remove any potential oxidizable substances from the bioburden reducing filter, the initial > 750 g of filtered placebo solution is collected immediately after the filter and discarded. When filtration is complete the holding tank is pressurized to 16 – 20 psia with nitrogen and cooled to $2 - 8\text{ }^{\circ}\text{C}$. The maximum allowable hold time in the holding tank is ≤ 72 hr.

2.3.P.3.3.3 Sterile Filtration and Filling

A pre-filtration bubble point integrity test is performed on the sterilizing $0.22\text{ }\mu\text{m}$ hydrophilic cartridge filter prior to equipment set-up. The holding tank is transferred to a controlled but unclassified area outside of the Class A filling area. The holding tank outlet valve is connected to the sterilizing $0.22\text{ }\mu\text{m}$ filter located in the Class A area, which flows into a surge vessel. The holding tank is pressurized with filtered nitrogen to 18 – 22 psia ($3.3 - 7.3$ psig; ≤ 25 psig), the bottom valve of the holding tank is opened to allow placebo solution to pass through the sterilizing filter and fill the surge vessel.

To remove any potential oxidizable substances from the sterilizing filter, the initial $> 2,000$ mL of sterile filtered placebo solution is purged from the surge vessel. The surge vessel is refilled, and the sterile placebo solution is filled into 8 mL, Type I glass vials. The filler is equipped with an automated in-line non-destructive weight check scale that collects vial tare and gross weight to achieve fill weights within 1.016 ± 0.041 g.

Filled vials are partially stoppered on the filling line as they exit the filling area and are transported via transfer belt to the automated lyophilizer loading table. All transfer and automated loading system components are in a Class A area. The processing time from addition of WFI to the compounding tank to the last vial loaded into the lyophilizer is ≤ 96 hr.

2.3.P.3.3.4 Lyophilization

The lyophilizer shelves are cooled and controlled to 5 °C and loaded. Upon completion of the lyophilizer loading, the door is closed, and a fully automated cycle (Table 4) is initiated via the lyophilizer control system.

Table 4: Lyophilizer Cycle

| Step | Step Description | Cycle Setting |
|------|----------------------|----------------------|
| 1 | Product load temp | 5 °C |
| 2 | Product hold time | 60 min |
| 3 | Ramp down to | -40 °C |
| 4 | Ramp rate | 0.5 °C/min |
| 5 | 1st freeze hold time | 90 min |
| 6 | Annealing temp | -20 °C |
| 7 | Ramp rate | 0.5 °C/min |
| 8 | Annealing hold time | 120 min |
| 9 | Ramp down to | -40 °C |
| 10 | Ramp rate | 0.5 °C/min |
| 11 | 2nd freeze hold time | 90 min. |
| 12 | Primary vacuum | 100 µbar (75 µ) |
| 13 | Primary shelf temp | 0 °C |
| 14 | Ramp rate | 1.0 °C/min |
| 15 | Primary hold time | 10 hr |
| 16 | Secondary dry temp | 35 °C |
| 17 | Ramp rate | 0.5 °C/min. |
| 18 | Secondary vacuum | 100 µbar (75 µ) |
| 19 | Secondary hold time | 14.8 hr |
| 20 | Vacuum break | 800 mbar (11.6 psia) |
| 21 | Seat stoppers | 1900 psig |
| 22 | Hold temp | 5 °C |
| 23 | Hold pressure | Atmospheric |

When capping starts the vials are fed to the capper that is fitted with a “no stopper” and “high stopper” detector so that triggering either of these sensors will reject the vial. Capped vials are transported to a tray loader located in a non-classified area, loaded into trays, and palletized. The pallets are stored at 2 – 8 °C until visually inspected.

2.3.P.3.3.5 Visual Inspection

All vials are manually visually inspected by qualified inspectors.

2.3.P.3.4 Controls of Critical Steps and Intermediates

Table 5 provides the critical process parameters (CPP), which are operating parameters controlled during manufacturing of Placebo for Injection. Also included are in-process specifications (IPS), which are tests that confirm the placebo is acceptable to forward process (Table 6).

Table 5: Critical Process Parameters

| Critical Process Parameter | Limit |
|--|------------------|
| WFI temperature filled into compounding tank | 15 – 25 °C |
| pH of buffer after HCl addition | 7.2 – 7.6 |
| Bioburden reduction filter purge weight | > 750 g |
| Temperature of bioburden reduced holding tank | 2 – 8 °C |
| Sterile filtration pressure | ≤ 25 psig |
| Sterilization filter purge volume | > 2,000 mL |
| Fill volume per vial | 1.000 ± 0.040 mL |
| Placebo hold time (i.e., total time from addition of WFI to compounding tank to last vial loaded into lyophilizer) | ≤ 96 hrs |
| 2nd freeze hold time | 90 min |
| Primary vacuum | 100 µbar (75 µ) |
| Primary shelf temperature | 0 °C |
| Ramp rate | 1.0 °C/min |
| Primary hold time | 10 hrs |

WFI = Water for injection; psig = Pounds per square inch gauge

Table 6: In-Process Specifications for Manufacture of Placebo for Injection

| Parameter | Analytical Method | Acceptance Criteria |
|---|-------------------|--|
| Pre-sterile filtration bioburden TAMC and TYMC | USP <61> | ≥ 5 cfu/100 mL (Alert Limit) ≥ 10 cfu/100 mL (Action Limit) |
| Pre-sterile filtration endotoxin | USP <85> | ≥ 1.25 EU/mL (Action Limit) |
| Post-use membrane integrity test of sterilization filter | Bubble point test | ≥ 50 psig |

TAMC = Total aerobic microbial count; TYMC = Total yeast and mold count; psig = Pounds per square inch gauge;
 EU = Endotoxin units

2.3.P.3.5 Process Validation and/or Evaluation

Not applicable

2.3.P.4 CONTROL OF EXCIPIENTS

The excipients in Placebo for Injection comply with the current requirements of the United States Pharmacopoeia (USP) or National Formulary (NF) monographs. However, the acceptance limits for bacterial endotoxins of Mannitol USP and Sucrose NF are tighter than their respective monograph limits. In addition, a bacterial endotoxin limit for Tromethamine USP has been added. The acceptance criteria for bacterial endotoxins (USP <85>) for mannitol, sucrose, and tromethamine are included in [Table 7](#).

In addition, Hydrochloric Acid NF, used to manufacture a 1 N solution for pH adjustment, Water for Injection USP, which is the placebo compounding solvent, and Nitrogen NF, which is for vacuum neutralization, are used in the manufacture of Placebo for Injection.

Table 7: Bacterial Endotoxin Specifications of Excipients

| Excipient | Reference to Standards | Bacterial Endotoxin Limits |
|---------------------------|------------------------|-----------------------------|
| Mannitol | USP | < 2.5 IU/g (< 0.0025 IU/mg) |
| Sucrose | NF | < 2 IU/g (< 0.002 IU/mg) |
| Tromethamine ¹ | USP | ≤ 2.5 IU/g (≤ 0.0025 IU/mg) |

¹ Also referred to as tris(hydroxymethyl)aminomethane (i.e., TRIS).

2.3.P.5 CONTROL OF PLACEBO

2.3.P.5.1 Specifications

Placebo batches of are tested and must conform at release and throughout shelf-life to the specifications provided in [Table 8](#)

Table 8: Release Specifications, Placebo for Injection

| Test | Analytical Procedure | Acceptance Criteria |
|-----------------------------------|------------------------------------|---|
| Appearance and Description | | |
| Lyophilized Product | T-0023 | White cake |
| Reconstituted Solution | T-0023 USP <790> | Clear, colorless liquid Essentially free of visible particulates |
| Identity and Purity | | |
| SDS-PAGE | T-0133 | No protein content detected |
| General | | |
| Reconstitution Time | T-0057 | ≤ 120 seconds |
| pH of Reconstituted Solution | USP <791> (T-0019) | 7.1 – 7.7 |
| Water ¹ | USP <921> ² (T-0022) | Mean of 20 vials ≤ 2.0 %; no individual vial > 3.2 % |

| Test | Analytical Procedure | Acceptance Criteria |
|--|------------------------------------|--|
| Particulate Matter Particles $\geq 10\ \mu\text{m}$ Particles $\geq 25\ \mu\text{m}$ | USP <788> ³ (T-0033) | $\leq 6,000$ particles/vial ≤ 600 particles/vial |
| Safety | | |
| Bacterial Endotoxins | USP <85> ⁴ | ≤ 1.25 EU/mL |
| Sterility ⁵ | USP <71> ⁶ | No growth |

Ref. Std. = Reference standard; IU = International unit; HMW = High molecular weight; EU = Endotoxin unit

¹ Reported as % moisture

² Karl Fischer method

³ Light obscuration method

⁴ Kinetic chromogenic method

⁵ Container closure integrity testing (CCIT) is performed on stability in lieu of Sterility testing.

⁶ Membrane filtration method

2.3.P.5.2 Analytical Procedures

A list of analytical procedure numbers and titles used for release and stability testing of placebo are provided in [Table 9](#). Analytical procedures that reference the General Chapters of the USP are performed according to the compendial requirements and, therefore, are not included in the table.

Table 9: Analytical Procedures for Control of Placebo

| Analytical Procedure | Title of Analytical Procedure |
|----------------------|---|
| T-0023 | Appearance/Color/Clarity Test Procedure |
| T-0133 | SDS-PAGE Minigel Testing for Placebo |
| T-0057 | Reconstitution Time |
| T-0402 | Container Closure Integrity Test ¹ |

¹ Container Closure Integrity testing is used throughout stability in lieu of sterility testing.

2.3.P.5.3 Validation of Analytical Procedures

Method validations demonstrate suitability of analytical procedures used for release and stability testing of Placebo for Injection. Analytical method validations, as appropriate, have included accuracy, precision, specificity, detection limit, quantitation limit, linearity, and range. A list of qualification documents for performing drug product testing is provided in [Table 10](#).

Suitability reports of pharmacopoeia methods for testing drug product for pH (<791>), Water Determination (<921>), Subvisible Particulate Matter (<788>), Bacterial Endotoxins (<85>), and Sterility (<71>) are listed in [Table 11](#).

Table 10: Analytical Procedure Method Validation Reports for Placebo

| Analytical Procedure | Validation Report No. | Analytical Procedure Name |
|-----------------------------|------------------------------|---|
| T-0023 | QCMT-052813P ¹ | Appearance/Color/Clarity Test Procedure |
| T-0133 | QCTD-T0133-031616 | SDS-PAGE Minigel Testing for Placebo |
| T-0057 | QCMT-052813P ¹ | Reconstitution Time |
| T-0402 | QCMV-2010 | Container Closure Integrity Test |

¹ Validation reports were included in the Leukine Drug Product Alternative Testing Site Qualification Report QCMT-052813R Version 2.

Table 11: Pharmacopoeia Method Qualification Reports for Placebo

| Analytical Procedure | Qualification Report No. | Analytical Procedure Name |
|-----------------------------|---------------------------------|------------------------------------|
| USP <790> ¹ | 2022/01078/00 | Visible Particulates in Injections |
| USP <791> | QCMV-T0019-102913R | pH |
| USP <921> | QCMV-T0022-051314R | Water Determination |
| USP <788> ² | RPT-0141 | Particulate Matter in Injections |
| USP <85> ¹ | 2020/00923/00 | Bacterial Endotoxins Test |
| USP <71> ¹ | 2021/01341/01 | Sterility Tests |

NA = Not available


¹ Performed at Patheon.

² Performed at Nitto Avecia Pharma Services.

2.3.P.5.4 Batch Analysis

The Certificate of Analysis for the placebo batch B27094 is provided in [Figure 2](#).

Figure 2: Certificate of Analysis – Placebo for Injection



PARTNER
THERAPEUTICS

CERTIFICATE OF ANALYSIS

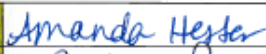

| Lyophilized Placebo Drug Product (Sucrose-Mannitol-Tris) | | | |
|---|-----------------------------|---------------------------|--|
| Material Number: 13131 | | Batch Number: B27094 | |
| Date of Manufacture: 28Jul2022 | Specification: SPEC-0019-00 | Effective Date: 18Aug2022 | |
| Partner Therapeutics Northpointe • 2625 162 nd St SW, Lynnwood WA 98087 • 425-245-1245 | | | |

| ASSAY | METHOD | SPECIFICATION | RESULTS |
|--|--------------------------|---|-------------------------|
| Appearance/Color/Clarity <ul style="list-style-type: none"> Lyophilized Product Reconstituted Solution | T-0023 | <ul style="list-style-type: none"> White cake. Clear, colorless liquid. | Pass |
| Appearance – Reconstituted Solution ¹ | USP <790> | <ul style="list-style-type: none"> Essentially free of visible particles | Pass |
| Test for Protein SDS-PAGE, Coomassie Stain | T-0133 | No protein content detected. | Pass |
| pH | USP <791> (T-0019) | 7.1-7.7 | 7.6 |
| Sterility Test ¹ | USP <71> | No growth | No growth |
| Endotoxin ¹ | USP <85> | ≤ 1.25 EU/mL | < 0.30 EU/mL |
| Water | USP <921> (T-0022) | Report the mean of 20 vials with no individual vial >3.2% | 1.1 % |
| Particulate Matter ² Particles ≥ 10 µm Particles ≥ 25 µm | USP <788> (T-0033) | ≤ 6000 particles/vial ≤ 600 particles/vial | 11 ≥ 10 µm 1 ≥ 25 µm |
| Reconstitution Time | T-0057 | ≤ 120 seconds. | 33 seconds |

¹ Performed at Patheon • 5900 Martin Luther King Jr Highway • Greenville, NC 27834 • (252) 758-3436

² Performed at Nitto AVECIA • 10 Vanderbilt • Irvine, CA 92618 • (949) 951-4425

The signatures below indicate that the results meet specifications

| | | | |
|--------------|---|-------|-----------|
| Compiled by: |  | Date: | 03NOV2022 |
| Approved by: |  | Date: | 04NOV2022 |

11/03/22 3:25 PM

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2.3.P.5.5 Characterization of Impurities

Not applicable.

2.3.P.5.6 Justification of Specifications

The specifications for placebo are based on absence of drug substance.

2.3.P.6 REFERENCE STANDARDS OR MATERIALS

The reference standard for testing placebo is the same reference standard used for testing drug substance sargramostim.

2.3.P.7 CONTAINER CLOSURE SYSTEM

The primary container closure system for Placebo for Injection consists of a clear, colorless, Type I borosilicate glass vial closed with a chlorobutyl stopper fastened by an aluminum crimp seal with a dark blue plastic flip-off cap. The description of the components of the primary packaging system (i.e., glass vials, stoppers, and aluminum seals), materials of construction, and manufacturer are listed in [Table 12](#).

Table 12: Description of Primary Packaging Components

| Description | Materials of Construction | Manufacturer |
|---|---|--|
| Clear, colorless, 20 mm glass vial | Tubing, Type I borosilicate glass | Ompi North America ¹ Canadá 130, Parque Nacional Industrial 65550 Ciénega de Flores, Nuevo Leon Mexico |
| Gray, 20 mm lyophilization stopper | 4432/50 chlorobutyl formulation, FluroTec® and B2 coating | West Pharmaceutical Services, Inc. Jersey Shore, PA 17740 United States |
| Aluminum seal with plastic dark blue flip-off cap | Aluminum and plastic | West Pharmaceutical Services of Florida, Inc. Clearwater, FL 33760 United States |

¹ Depending upon supply and product demand the vials may be manufactured by Nuovo Ompi S.r.l., Piombino Dese, Padova, 35017, Italy or Nuovo Ompi S.r.l., Borgo Tor Tre Ponti, Latina, 04013, Italy.

The glass vials (6R) are manufactured in compliance with ISO 9001:2008, Quality Management Systems, and meet the requirements of the USP General Chapter <660>, Containers-Glass. The specifications for the clear, colorless Type I glass vials manufactured by Ompi North America are provided in [Table 13](#).

Table 13: Glass Vials (Dimensions: 22 mm x 40 mm) Specifications

| Test | Test Method | Acceptance Criteria |
|------------|--------------------|---------------------|
| Appearance | Visual examination | Clear, colorless |
| Volume | USP <660> | ≥ 5.0 and ≤ 10.0 mL |

| Test | Test Method | Acceptance Criteria |
|---|--------------------|---|
| Alkaline Release | USP <660> | ≤ 1.0 mL 0.01 M HCl |
| Dimensions Body Diameter Collar Diameter Neck Diameter Collar Height Neck Height | COC | 21.80 – 22.20 mm 19.70 – 20.20 mm 0.00 – 16.50 mm 3.40 – 3.80 mm 8.00 – 9.00 mm |
| Glass type | Glass Supplier COA | Borosilicate type I |

COC = Certificate of Conformance; COA = Certificate of Analysis

The chlorobutyl stoppers meet the requirements of the USP General Chapter <381>, Elastomeric Closures for Injections. The specifications for the gray, chlorobutyl stoppers manufactured by West Pharmaceutical Services are provided in [Table 14](#).

Table 14: Chlorobutyl Stopper (Formulation: 4432/50) Specifications

| Test | Test Method | Acceptance Criteria |
|--|--------------------|--|
| Appearance | Visual examination | Gray |
| Total Bioburden | USP <61> | ≤ 12.09 cfu/20 stoppers ≤ 5 cfu/100 m ² |
| Bacterial Endotoxin | USP <85> | ≤ 0.10 EU/mL/10 stoppers ≤ 1.0 EU/stopper |
| Particulates > 25 – 50 μ > 50 – 100 μ > 100 μ | QC | ≤ 13.0 particles/10 cm ² ≤ 3.5 particles/10 cm ² ≤ 0.9 particles/10 cm ² |
| Elastomer Type | Supplier COA | Chlorobutyl 4432/50 |

cfu = Colony forming units; EU = Endotoxin units; QC = Quality Certificate

The specifications for the aluminum seals manufactured by West Pharmaceutical Services are provided in [Table 15](#).

Table 15: Aluminum Seals (Size: 20 mm) Specifications

| Test | Test Method | Acceptance Criteria |
|----------------|--------------------|---------------------------|
| Appearance | Visual examination | Silver with dark blue cap |
| Flip-off Force | QC | 3.6 – 5.4 lbs. |
| Overall Height | QC | 0.370 – 0.394 in. |
| Skirt Length | QC | 0.293 – 0.291 in. |

QC = Quality Certificate

2.3.P.8 STABILITY

2.3.P.8.1 Stability Summary and Conclusions

Stability data on Placebo for Injection, previously manufactured at Pfizer, McPherson, Kansas, USA support a 60-month expiry when stored at refrigerated conditions (2 – 8 °C).

2.3.P.8.2 Postapproval Stability Protocol and Stability Commitment

Placebo batches will be tested according to the protocol provided in [Table 16](#).

Table 16: Stability Protocol (2 – 8 °C)

| Test | Timepoint (months) | | | | | |
|---|--------------------|----|----|----|----|----|
| | 0 ¹ | 12 | 24 | 36 | 48 | 60 |
| Appearance – Lyophilized (T-0023) | x | x | x | x | x | x |
| Appearance – Reconstituted (T-0023) | x | x | x | x | x | x |
| pH of Reconstituted Solution (T-0019) | x | x | x | x | x | x |
| Water (T-0022) | x | x | x | x | x | x |
| Particulate Matter (T-0033) | x | -- | x | x | x | x |
| Container Closure Integrity (T-0402) ² | x | -- | x | x | x | x |

¹ Zero (0) timepoint is the release result

² Performed in lieu of sterility

2.3.P.8.3 Stability Data

The placebo batch B27094 has been placed on long-term stability studies, October 2022, according to the protocol provided in [Table 16](#). Currently, the stability data is unavailable.