Template

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Not Responsible for Investigator's Use

Standard Operating Procedure

Form-Q111

Filter Integrity Test by Bubble Point

1. **Purpose:** To describe the procedure for integrity testing a sterile filter using bubble-point determination.

2. **Scope:** The last step in the manufacturing process requires sterile filtration of the final product. Integrity testing of the sterile filter post-filtration adds another level of assurance that the product is sterile. This procedure is one of the tests performed after the manufacturing is complete, and it must be completed prior to releasing the lot for human administration.

3. **Responsibilities:**
   3.1 To follow this procedure as written and to ensure that all results, control information, and raw data are documented as specified in the corresponding Master Production & Batch Records for this lot.

4. **References**
   4.1 USP 28 ‹821› Radioactivity
   4.2 USP 28 ‹823› Radiopharmaceuticals For Positron Emission Tomography—Compounding
   4.3 **Form-Q015**, "Investigating Out of Specification QC Test Results"
   4.4 **FDA Draft Guidance PET Drug Products—Current Good Manufacturing Practice (CGMP)—September 2005 (CDER)**

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4.5 Manufacturer's Specifications for Integrity Test
4.6 **Form-Q108**, "Resterilization of Final Product in the Event of a Failed Filter Integrity Test"
4.7 **Form-M120,** "Documentation of Manufacturing Variances**"**

5. Forms

- **Form MVR-001**, Manufacturing Variance Report Form
- **Form IOS-001**, Investigating Out of Specification (OOS) QC Test Results Form

6. Policies

6.1 Perform the procedures using good radiation safety techniques, as the filter will contain residual radioactive product.

7. Materials and Equipment

7.1 Nitrogen Gas, Compressed Air, or Air in a Syringe
7.2 Pressure Test Apparatus (modified Nalgene Bubble Point Test Apparatus)
7.3 Beaker
7.4 Water
7.5 Filter to be Integrity Tested (still wet from use)

8. PROCEDURES

8.1 Integrity Test of the Filter

8.1.1 After passing 10-30 mL of water place the filter in the filter case of the Nalgene Bubble Point Apparatus and tighten in place. Introduce 3-5 ml of water in the filter outlet tube of the apparatus.

8.1.2 Slowly increase the applied pressure to the setup while observing the water for any emerging bubbles from the filter outlet.

NOTE: Initially a few bubbles may appear, however, they should cease as the pressure is increased.

8.1.3 Continue increasing the pressure on the filter until a slow stream of bubbles begins to emerge from the filter outlet, **OR** until the pressure exceeds 50 psig. Record the pressure at which bubbles appeared, or "≥ 50 psig" if pressure exceeded 50 psig without development of bubbles, as the filter bubble point.

8.1.4 Compare the wet filter bubble point to the manufacturer's specification (≥ 46 psig for a PALL PN4612.)

8.1.5 If the test yields a bubble point lower than the wet filter bubble point specification, pass approximately 10-30 mL of water through the filter to insure that it is completely wet and repeat the test. T he filter must be completely wet to perform an accurate integrity test.

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NOTE: If re-wetting is necessary, document on **Form MVR-001**, "Manufacturing Variance Report Form."

8.2 Acceptance Criteria

8.2.1 The measured wet filter or re-wetted filter bubble point *must be equal to or greater than* the manufacturer's specification.

8.2.2 If the filter fails the bubble point test and the product is refiltered using a new filter, the *new filter must pass the bubble point test* and *its bubble point must be equal to or greater than* the manufacturer's specification.

8.3 Failure to Pass the Bubble Point Test

8.3.1 If the *original filter has a bubble point less than* the manufacturer's specifications, and *it also fails the bubble point test after rewetting*, perform Resterilization of the Final Product as per **Form-Q108**, "Resterilization of Final Product in the Event of a Failed Filter Integrity Test," and document the integrity test failure and manufacturing variance on **Form MVR-001**, "Manufacturing Variance Report Form," and place with the corresponding batch record.

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