Q.I. Medical, Incorporated
Pharmacy IV Admixture QA Procedures

A guide to monitoring of work area environmental conditions, validation of aseptic technique, and sterility and pyrogen testing

Environmental Monitoring

Air sampling using volumetric collection methods shall be performed at least semiannually, usually as part of the re-certification of facilities and equipment. Refer to "Environmental Viable Airborne Particle Testing Program", USP General Chapter <797> Pharmaceutical Compounding – Sterile Preparations, effective 6/1/2008.

Air Sampling – Supplemental testing between re-certifications using EnviroTest

1. Carefully remove EnviroTest paddles from their protective tubes just before using. Place one (1) EnviroTest in each work area of each Laminar Air Flow Workbench (LAFW) or barrier isolator to be monitored. Position each EnviroTest at least 6 inches inside the work area. EnviroTests should be centered in work areas, with the agar surface perpendicular to the normal unimpeded air flow.

   If the LAFW or isolator is located in a "clean room", place an additional (1) EnviroTest outside of the LAFW. A location inside the clean room but near the entrance is preferred.

2. Expose EnviroTest agar to airflow for approximately one (1) hour. If the agar appears excessively dry after one hour, decrease exposure time to one half (½) hour.

3. Replace paddles into protective tubes. Place completed gummed label on cap of EnviroTests.

4. Incubate #ET1000 at 30-35^{O}C for 48 to 72 hours. Incubate #ET3000 at 26-30^{O}C for 120 to 168 hours. Record results in log. (0 CFU's is normal)

Surface Testing

5. Remove one (1) EnviroTest paddle from protective tube. Gently rock and press surfaces of agar against selected areas in the LAFW or isolator, at least 6 inches inside the work area. Note: Do not slide agar across work surface.

6. Replace paddle into protective tube. Place completed gummed label on cap of EnviroTest.

7. Incubate #ET1000 at 30-35^{O}C for 48 to 72 hours. Incubate #ET3000 at 26-30^{O}C for 120 to 168 hours. Record results in log. (0 CFU's is normal)

Maintenance Protocol - Perform tests at least monthly in areas used to prepare low and medium-risk compounds and at least once per week in areas used to compound high-risk preparations.

1. Follow steps 1 through 7 above. Log results by location and note any trends over time.

2. Review Table 4 in USP Chapter <797> for recommended action levels.

3. If colony forming units (CFUs) counts exceed guidelines, check HEPA filters, room air sources, cleaning solutions/protocols, equipment used in the hood, and other possible sources of the increased contamination. Immediately begin appropriate decontamination procedures with the aid of a microbiologist or infection control professional.

Gloved Fingertip Sampling

1. Collect gloved fingertip and thumb samples from both hands immediately after completing the hand hygiene and garbing procedure. New compounders must successfully (0 cfu) complete this test three times before being allowed to prepare CSPs for human use.

2. Collect gloved fingertip and thumb samples from both hands immediately after completing any media-fill test procedure. Do not disinfect gloves prior to sampling.

3. Incubate #ET1000 at 30-35^{O}C for 48 to 72 hours. Incubate #ET3000 at 26-30^{O}C for 120 to 168 hours. Record results in log.

Personnel & Process Validation using Media-Fill Testing

Startup Protocol - Use to: (1) validate current pharmacists and technicians who manipulate sterile IV admixtures and (2) validate each newly hired staff member before they begin performing any manipulation requiring impeccable aseptic technique.

1. Choose a procedure that most closely simulates frequently used, complex, manipulations that are or will be performed by the pharmacy staff member. Directions for Use (DFU) that come with GroMed Personal Aseptic Technique Tests, PATT and PATT2, are suggestions and can be modified to fit a particular pharmacy's policies.

2. **Low-Risk:** PATT kits (#GM7020 & GM7030) exceed the challenge level required for a media-fill test procedure for low-risk level compounding.

3. **Medium-Risk:** PATT kits (#GM7020 & GM7030) exceed the challenge level required for a media-fill test procedure for medium-risk level compounding.

4. **Medium-Risk, Increased Challenge:** Perform the steps suggested in the Directions for Use for the PATT or PATT2. Using a standard sterile pharmacy tubing set, use gravity to transfer the final contents of the bag of TSB into either an empty vial or bag.

5. **Medium-Risk Process Simulation:** Pharmacies that routinely use automated compounders can simulate common, complex process. Use bags (up to 500 mL) and vials of GroMed TSB media to substitute for both large and small volume liquid components. Typical medium-risk simulations with GroMed media include creating TPN and cardioplegia admixtures.

6. **High-Risk:** Follow all the steps described in the PATT or PATT 2 directions for use.

7. Dissolve 3 grams of Soybean-Casein Digest Media, GroMed #GM3000, in 100 mL of non-sterile water.

8. Draw 10 mL of the nonsterile TSB into a 20 mL syringe. Attach a 0.2µ syringe filter and sterile needle to the syringe.

9. Inject 10 mL of sterilized TSB into the bag. Label and incubate as described in the PATT or PATT2 directions for use.

Maintenance Protocol - Perform at least annually for low-risk level, annually or more frequently for medium-risk level and semiannually for high-risk level, or whenever unacceptable technique is observed.

1. Duplicate the procedure(s) used to initially validate the staff member. The number of repetitions of the basic manipulation may be reduced during revalidation if approved by the pharmacy manager. The procedure must be successfully completed without contamination. Any validation procedure that yields a positive result must be repeated until no positives are observed.

2. Positives should be analyzed to determine the probable break in aseptic technique that lead to the contamination. Conduct additional training and supervise as necessary to improve the individual's aseptic technique.

3. Record results in the log provided in each GroMed case. Optional - Enter results in the individual's personnel record.

Admixture End Product Testing - Sterility

Startup and Maintenance Protocol - Test targeted admixtures according to USP <797>, Sterility Test". Minimum test frequency is determined by batch size, multiple patient risk, and time/temperature exposure. The membrane filtration method is the method of choice where feasible. **All sterility tests should begin within 60 minutes of admixture preparation.**

1. Choose the QuickTest, QT Junior, or QTMicro that will test the complete admixture with the least amount of manipulation.

2. Pass admixture to be tested through the filter. For maximum sensitivity to the many potential sources of contamination, all of the LVP & SVP components should pass through the filter either during or within 60 minutes after completion of the admixing procedure being validated. Follow the Directions For Use (DFUs) enclosed in each case of testers.

3. Introduce GroMed media into filter chamber. Note for QuickTests: Admixtures containing fat emulsions may cause the TSB media to appear slightly cloudy. If necessary, use the extra GroMed media provided to rinse the filter of residual fat emulsion.

4. Complete and attach the gummed label to the filter housing.

5. Incubate the QuickTest, QTJunior, or QTMicro testers containing TSB at 22+/-2.5^{O}C, testers containing FTM at 32.5+/-2.5^{O}C, for not less than 14 days. If the media becomes turbid before 14 days the test is "Positive". Further observation is not necessary.

6. Positive tests should be investigated to locate the probable source of the admixture contamination. To help determine the source of accidental contamination, a positive tester may be sent to a microbiology laboratory to perform a species identification of the microorganism.

7. A "Negative" test may contain slow growing fungi. A blind secondary culture test for slow growing fungi can be performed using Potato Dextrose Agar (PDA) slants, GroMed #GM4000. Follow the directions supplied in each box of PDA slants.

8. Fluid Thioglycollate (FTM) is available separately in a variety of containers for use in performing sterility tests using two medias. For more details refer to the Q.I. Medical web site: http://www.qimedical.com/pricelist.htm

Admixture End Product Testing - Endotoxins

Startup Protocol - Use to ensure that each lot of nonsterile drug components in inventory do not exceed specified endotoxin limits.

1. Review the PyroTest Directions for Use (DFU). Verify that (1) the PyroTest is appropriate per the "Intended Use", (2) the drug(s) to be tested are compatible with gel-clot endotoxin testing, and (3) if the U.S. Pharmacopeia has assigned an endotoxin release limit.

2. Using the drug's master work sheet and preparation work sheet, compound a small quantity of the drug to be tested. Compound the most commonly prescribed concentration.

3. Follow the appropriate PyroTest dilution procedure. Incubate the Assay and Positive Control Vials undisturbed for 60 minutes at $37^{O}C$.

4. Positive results in the Assay Vial indicate the test sample contains more than the maximum allowable endotoxin.

Maintenance Protocol - Use this maintenance protocol after the nonsterile drug components in inventory have been tested and shown to contain endotoxin levels below acceptable levels.

1. Perform endotoxin test upon receipt of each new lot of bulk, nonsterile drug components.

2. Perform endotoxin test on each batch of finished sterile drug products if the batch size, multiple patient risk, or time/temperature exposure criteria are exceeded according to USP <797>, Bacterial Endotoxin (Pyrogen) Testing.

3. Use professional judgement regarding endotoxin testing when the preparation of a drug product is rare and/or the medical need is immediate.

4. Carefully follow the PyroTest DFUs. Always check the U.S. Pharmacopeia for updates to a drug's endotoxin release limit.

5. Incubate the Assay and Positive Control Vials in the PyroTest incubator block, #INC004, undisturbed for 60 minutes at $37^{0}C$.

6. Follow pharmacy's policy for quarantine and release from quarantine of covered drug products.

Pharmacy IV Admixture QA Procedures

Product Needs Analysis

Environmental Monitoring

EnviroTests needed to support Maintenance Protocol

Number of hoods/isolators to monitor =_____

Times 2 EnviroTests per hood (1 air + 1 surface) X 2 =_____

Plus 1 EnviroTest per clean room +1 =_____

Times #_____ of monitoring days per month X Days/month =_____ #EnviroTests needed / month

Gloved Finger Tip Sampling

EnviroTests needed to support Startup and Periodic Sampling

Number of Staff to sample, initial evaluation (3 tests/staff) =_____

Number of Staff to sample after each aseptic technique test =_____

Personnel & Process Validation

GroMed media needed to support Startup and Maintenance Protocol

Number of Pharmacists & Technicians to validate =_____

Low Risk: #_____ PATT Kits per validation =_____ PATT Kits needed

Medium/High Risk: #_____ PATT Kits per validation =_____ PATT Kits needed

Medium/High Risk: #_____ containers of media per validation =_____Vials & _____ Bags needed

Admixture End Product Testing - Sterility

QuickTest, Junior, & Micro filter units needed to support Startup and Maintenance Protocol

Total number of targeted admixtures prepared per month =_____

Admixture End Product Testing - Endotoxin

PyroTests needed to support Startup Protocol

Number of in-stock drug components to test =_____

PyroTests needed to support Maintenance Protocol

Number finished batches/doses of drugs to test =_____