



HardyVal™ CSP MEDIUM-RISK LEVEL MEDIA-FILL CHALLENGE KITS

[Cat. no. HVM1](#) Medium-Risk Level Media-Fill Comprehensive Challenge Test Kit - Bag Single-Use Kit

Each kit contains:

| | |
|--|---------|
| Tryptic Soy Broth (TSB), 1000ml Dual Port Bag, 700ml | 1 bag |
| Sterile 100ml Dual Port Bags (empty) | 6 bags |
| Sterile 20ml Serum Vials (empty) | 6 vials |
| Whirl-Pak® Bag | 1 bag |
| Results Log Sheet | 1 sheet |

[Cat. no. HVM2](#) Medium-Risk Level Media-Fill Basic Challenge Test Kit - Vials Single-Use Kit

| | |
|--|---------|
| Tryptic Soy Broth (TSB), 50ml Serum Vial, 50ml | 3 vials |
| Sterile 50ml Serum Vials (empty) | 6 vials |
| Sterile 20ml Serum Vials (empty) | 3 vials |
| Whirl-Pak® Bag | 1 bag |
| Results Log Sheet | 1 sheet |

[Cat. no. HVB5](#) Tryptic Soy Broth (TSB), USP, 1L IV Bag, 700ml 5 bags

INTENDED USE

Hardy Diagnostics HardyVal™ CSP Medium-Risk Level Media-Fill Challenge Test Kits are recommended for routine use in the monitoring of proficiency testing and aseptic procedures used in Compounding Sterile Preparations (CSPs). Each kit contains the necessary materials for one pharmacist or technician to perform the annual medium-risk level media-fill challenge testing as specified in USP Chapter <797>.

This product is not intended to be used for the diagnosis of human disease.

SUMMARY

On January 1, 2004 Chapter <797>, of the United States Pharmacopeia/National Formulary (USP27/NF22) entitled "Pharmaceutical Compounding Sterile Preparations", became effective. USP Chapter <797> details the procedures and requirements for compounding sterile preparations and sets standards that are applicable to all practice settings in which sterile preparations are compounded. Since USP Chapter <797> is considered a requirement, pharmacies may be subject to inspection for compliance with these standards by State Boards of Pharmacy, the FDA, and accreditation organizations, such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), Accreditation Commission for

Health Care, Inc. (ACHA) and the Community Health Accreditation Program (CHAP). Compliance with these standards was required by January 1, 2006.

USP Chapter <797> defines three levels of risk related to sterile preparation and includes quality assurance requirements for each risk level. These risk levels are based on the potential for introducing sources of contamination to the preparations from microbial, chemical or physical contamination during compounding activities, or in the case of high-risk compounding, that the product would remain contaminated. USP Chapter <797> provides general guidance on risk level assignment based upon compounding manipulations, types of ingredients and equipment used, compounding environment, and storage and use of the resulting preparation. A summary table of risk levels is included below however, regardless of the examples provided, *the ultimate determination of risk level is the responsibility of the licensed health care professionals who supervise compounding, using their professional judgement and experience.*

The HardyVal™ CSP Medium-Risk Level Media-Fill Challenge Test Kit is available in two formats: The Comprehensive Challenge Test Kit (with IV bags) and the Basic Challenge Test Kit (without IV bags, with serum vials only). The HardyVal™ Tryptic Soy Broth (TSB), USP one liter IV bag is also available as a standalone component.

| Risk Level | Description | Examples | QA Monitoring and Frequency |
|---------------|--|---|--|
| Low | <ul style="list-style-type: none"> Involves only transfer, measuring and mixing with closed or sealed packaging systems. Limited to aseptically opening ampules, penetrating sterile stoppers on vials with sterile needles or syringes, transferring sterile liquids in sterile syringes to sterile administration devices. Prepared entirely in an ISO Class 5 (see below) or better air quality environment. In the absence of passing a sterility test, storage for a maximum of 48 hours at room temperature, 14 days refrigerated, or 45 days in solid frozen state. | <ul style="list-style-type: none"> Single transfers of sterile dosage forms from ampules, bottles, bags, and vials using sterile syringes with sterile needles. (<i>Vancomycin 1gm in NS 100ml prepared for 1 patient.</i>) Manually measuring and mixing no more than 3 manufactured products to compound drug admixtures and nutritional solutions. (<i>TPN solution compounded using gravity transfer of commercially available sterile Amino Acid and Dextrose solutions, and no more than 3 sterile additives transferred using a syringe and needles.</i>) | <p>Media-Fill Challenge Test <i>Low-risk Media-fill Challenge</i> <u>Hardy Cat. no.:</u> HVL1 <u>Frequency:</u> Annual testing for each person who compounds low-risk sterile preparations.</p> <p>Environmental monitoring: <i>Air Monitoring:</i> <u>Hardy Cat. nos.:</u> G60, 5533 <u>Frequency:</u> At least semi-annual testing of each Laminar Air Flow Workbench or barrier isolator.</p> <p><i>Surface and Glove Fingertips:</i> <u>Hardy Cat. no.:</u> P34 <u>Frequency:</u> Surface monitoring required on a periodic basis of each Laminar Air Flow Workbench or barrier isolator. Glove fingertips shall be done at initial competency evaluation and no less than three times before being allowed to compound sterile preparations. Re-evaluation is required at each media fill challenge test.</p> |
| Medium | <ul style="list-style-type: none"> Multiple individual or small doses are combined or pooled to prepare a CSP for administration to multiple patients or to one patient on multiple occasions. Involves complex aseptic manipulations or requires a long duration to prepare. Does not contain broad-spectrum bacteriostatic substances, and is administered over several days (e.g. worn or implanted infusion device). Prepared entirely in an ISO Class 5 (see below) or better air quality environment. In the absence of passing a sterility test, storage for a maximum of 30 hours at room temperature, 9 days refrigerated, or 45 days at solid frozen state. | <ul style="list-style-type: none"> TPN fluids using manually or automated compounded, involving multiple injections, detachments, and attachments of nutrient source products to deliver components to a final sterile container. Filling reservoirs of injection and infusion devices with multiple sterile drug products and evacuation of air from those reservoirs before dispensing. (<i>Chemotherapy prepared for infusion over 5 days using a portable infusion device.</i>) Filling reservoirs of injection and infusion devices with sterile drug solutions that will be administered over several days at ambient temperatures between 25° and 40°C. (<i>Implanted pump reservoir filled with Preservative-Free Morphine for infusion over 4 weeks.</i>) Transfer from multiple ampules or vials into a single, final sterile container or product. (<i>Any IV solution compounded with more than 3 additives.</i>) | <p>Media-Fill Challenge Test <i>Medium-risk Media-fill Challenge</i> <u>Hardy Cat. no.:</u> HVM1 and HVM2 <u>Frequency:</u> Annual testing for each person who compounds medium-risk sterile preparations.</p> <p>Environmental Monitoring: <i>Air Monitoring:</i> <u>Hardy Cat. no.:</u> G60 <u>Frequency:</u> At least semi-annual testing of each Laminar Air Flow Workbench or barrier isolator.</p> <p><i>Surface and Glove Fingertips:</i> <u>Hardy Cat. no.:</u> P34 <u>Frequency:</u> Surface monitoring required on a periodic basis of each Laminar Air Flow Workbench or barrier isolator. Glove fingertips shall be done at initial competency evaluation and no less than three times before being allowed to compound sterile preparations. Re-evaluation is required at each media fill challenge test.</p> |
| High | <ul style="list-style-type: none"> Non-sterile ingredients are incorporated or a nonsterile device is employed before terminal sterilization. Non-sterile ingredients are incorporated, or a non-sterile device is employed before terminal sterilization. Non-sterile components are exposed for at least 6 hours before being sterilized. Exposed to air quality inferior to ISO Class 5 (see below). In the absence of passing a sterility test, storage for a maximum of 24 hours at room temperature, 3 days refrigerated, or 45 days in solid frozen state. | <ul style="list-style-type: none"> Dissolving non-sterile bulk drug and nutrient powders to make solutions which will be terminally sterilized. (<i>TPN solutions made from dry amino acids.</i>) Measuring and mixing sterile ingredients in non-sterile devices before sterilization is performed. (<i>Ophthalmic solution filtered into a non-sterile dropper bottle.</i>) | <p>Media-Fill Challenge Test <i>High-risk Media-fill Challenge</i> <u>Hardy Cat. no.:</u> HVH1 <u>Frequency:</u> Semi-annual for each person who compounds high-risk sterile preparations.</p> <p>Environmental: <i>Air Monitoring:</i> <u>Hardy Cat. no.:</u> G60 and W28 <u>Frequency:</u> At least semi-annual testing of each Laminar Air Flow Workbench or barrier isolator.</p> <p><i>Surface and Glove Fingertips:</i> <u>Hardy Cat. no.:</u> P34 <u>Frequency:</u> Surface monitoring required on a periodic basis of each Laminar Air Flow Workbench or barrier isolator. Glove fingertips shall be done at initial competency evaluation and no less than three times before being allowed to compound sterile preparations. Re-evaluation is required at each media fill challenge test.</p> |

Source of risk level information: www.uspnf.com

Training for personnel who compound sterile preparations is mandatory and should be comprehensive and include thorough evaluation. Media-fill challenge testing (media-fill verification of technique) is used to verify that personnel have the necessary skills to compound sterile preparations. During media-fill challenge testing, personnel are instructed to prepare a CSP using sterile liquid culture medium. The resulting solution is then incubated at 25-35°C for 14 days. The solution is examined for the evidence of microbial growth or turbidity during incubation and at the end of the 14 day period. If there is evidence of turbidity, the challenge test has failed and it can be concluded that there was a breach in aseptic technique.

All personnel who compound CSPs must complete media-fill challenge testing before they are allowed to compound CSPs. As specified in the USP Chapter <797>, quality assurance procedures for medium-risk level CSPs include all of the procedures specified for low-risk CSPs, as well as a more challenging media-fill test passed annually or more frequently.

Tryptic Soy Broth, the medium used in the media-fill challenge testing, is widely used for the cultivation of microorganisms from environmental sources supporting the growth of the majority of bacteria and fungi. Tryptic Soy Broth, also known as TSB or Soybean-Casein Digest Broth, conforms to the formula given by the U.S. Pharmacopeia.⁽¹⁾ This medium contains digests of soybean meal and casein, which provide amino acids and other nitrogenous substances, making it a highly nutritious medium for a variety of organisms. Sodium chloride is added to maintain the osmotic equilibrium. Dextrose is incorporated as an energy source. The dipotassium phosphate is included in the formulation as a buffer to maintain the proper pH.

FORMULA

Ingredients per liter of deionized water:*

| | |
|-------------------------------|--------|
| Pancreatic Digest of Casein | 17.0gm |
| Sodium Chloride | 5.0gm |
| Papaic Digest of Soybean Meal | 3.0gm |
| Dextrose | 2.5gm |
| Dipotassium Phosphate | 2.5gm |

Final pH 7.3 +/- 0.2 at 25°C

*Adjusted and/or supplemented as required to meet performance criteria.

STORAGE AND SHELF LIFE

Storage: Upon receipt store at 2-25°C away from direct light. Media should not be used if there are any signs of deterioration (discoloration), contamination, or if the expiration date has passed. Protect from light, excessive heat, moisture, and freezing.

The expiration date on the product label applies to the product in its intact packaging when stored as directed.

Refer to the document "[Storage](#)" for more information.

PRECAUTIONS

This product is for laboratory use only. Not for injection or ingestion. Observe approved biohazard precautions and aseptic techniques. This product is to be used only by adequately trained and qualified personnel. Sterilize all biohazard waste before disposal.

Refer to the document "[Precautions When Using Media](#)" for more information.

PROCEDURE

When performing media-fill risk fill challenges, use procedures and techniques that most closely resemble those used during routine compounding of Medium-Risk Level CSPs. If necessary, the following procedure may be modified to include more complex manipulations. Once begun, the test is completed without interruption.

HVM1 – Comprehensive Challenge

1. Label the empty sterile 20ml vials with the date the challenge is performed and the initials of the person performing the procedure.
2. Within an ISO Class 5 air quality environment, aseptically transfer six aliquots of approximately 100ml of sterile Tryptic Soy Broth (by using the white conical male adapter port or using a sterile 100ml syringe and 18-gauge needle) into the separate empty sterile 100ml bags. To access the gravity tubing port on the large bag, twist off the top of the butterfly closure (see **Figure 1**). Once opened and connected to tubing, the butterfly port will remain open with a continuous flow of media. To access the needle-port septum, apply gentle pressure to the tip of the male adapter port until it snaps off. Media can be dispensed as desired via syringe transfer using the needle-port septum. To access the gravity tubing port on the small bags, gently apply pressure to the side of the tip of the male adapter until it snaps off. **Note:** *Lines on the bags are approximate and are not for accurate measuring.*
3. Arrange the six bags into three pairs.
4. Using a sterile 10ml syringe and 18-gauge needle, aseptically remove a 5ml aliquot from the first small bag in a pair and transfer it to the second small bag in the pair.
5. Agitate the second small bag for 10 seconds and then aseptically remove a 5ml aliquot and return it to the first small bag in the pair.
6. Agitate the first small bag for 10 seconds and then aseptically remove a 5ml aliquot from the first small bag and transfer it to the second small bag in the pair.
7. Following the exchanges, using a sterile 10ml syringe and vented needle, aseptically remove a 5ml aliquot from each small bag in the pair and transfer it to one separate glass vial.
8. Repeat steps 4 through 7 for the other two remaining pairs.

9. Apply sterile adhesive seals aseptically to the rubber closures once the vials have been filled.
10. Place the six vials (from step 7) into a Whirl-Pak® bag for transport to the incubator.
11. Discard all needles and syringes into a biohazard sharps container.
12. Incubate the vials at 20-25°C and/or 30-35°C for 14 days. If two temperatures of incubation are selected, incubate for 7 days at each temperature.
13. Examine for the presence of turbidity. *Note: Growth may not be evenly dispersed throughout the vial. Tap or swirl the vial to observe for growth that may have settled at the bottom.* If growth is observed the vial may be discarded and it is not necessary to continue incubating for the full 14 days.
14. Record results on the “Results Log Sheet”.
15. Discard all completed test vials and bags as biomedical waste.

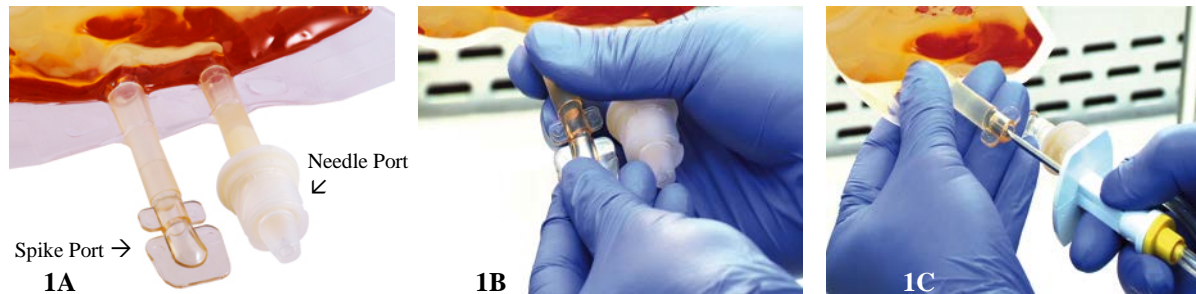


Figure 1. A) The large bag has two tails, one with a butterfly closure (left) for use with gravity tubing and another with a removable white conical male adapter closure (right) for performing needle-port syringe transfers. Apply gentle pressure to the tip of the male adapter port (right) until it snaps off to expose the needle-port septum. B) Twist the bottom part of the butterfly closure to remove and gain access with the plastic spike needle to the gravity tubing port. C) Insert needle and gravity tubing into the opened port to create a continuous media flow into the 100ml bag.

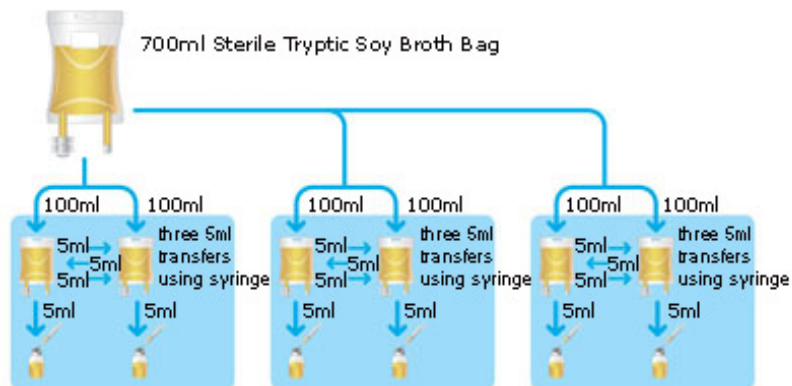


Figure 2. A graphic display of the HardyVal Medium Risk assessment. *This is an example procedure and does not necessarily reflect the procedure that every customer should use. Please refer to the guidelines detailed by your regulatory body to determine the best testing procedure for your laboratory.*

HVM2 – Basic Challenge

1. Label the empty sterile 20ml vials with the date the challenge is performed and the initials of the person performing the procedure.
2. Within an ISO Class 5 air quality environment, arrange the three vials containing 50ml of TSB. Arrange the six empty 50ml vials into three pairs.
3. Using a separate 18-gauge needle and syringe for each pair, aseptically transfer two aliquots of approximately 25ml of sterile Tryptic Soy Broth into each of the empty sterile 50ml vials. Repeat this process with fresh tubing or a fresh syringe 2 more times so that there will be six 50ml vials containing 25ml of test media.
4. Using a sterile 10ml syringe and 18-gauge needle, transfer one 5ml aliquot of medium from the first vial to the second vial in the pair.
5. Agitate the second vial for 10 seconds and then aseptically remove a 5ml aliquot and return it to the first vial in the pair.
6. Agitate the first vial for 10 seconds and then aseptically remove a 5ml aliquot from the first vial and transfer it to the second vial in the pair.
7. Following the exchanges, using a sterile 10ml syringe and vented needle, aseptically remove a 5ml aliquot from each container in the pair and transfer it to one empty sterile 20ml vial.
8. Repeat steps 4 through 8 for the other two remaining pairs.
9. Apply sterile adhesive seals aseptically to the rubber closures once the vials have been filled.
10. Place the three vials (from step 4-8) into a Whirl-Pak® bag for transport to the incubator.
11. Discard all needles and syringes into a biohazard sharps container.
12. Incubate the vials at 20-25°C and/or 30-35°C for 14 days. If two temperatures of incubation are selected, incubate for 7 days at each temperature.
13. Examine for the presence of turbidity. **Note:** *Growth may not be evenly dispersed throughout the vial. Tap or swirl the vial to observe for growth that may have settled at the bottom.* If growth is observed the vial may be discarded. Do not continue to incubate for the full 14 days.
14. Record results on the “Results Log Sheet”.
15. Discard all completed test vials as biomedical waste.

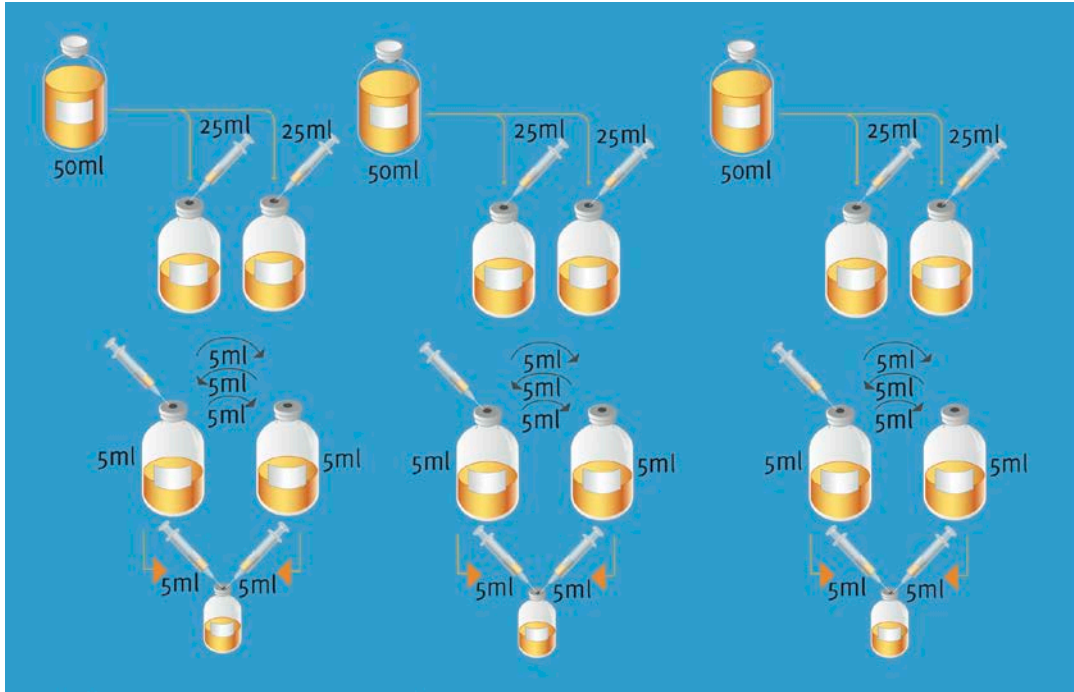


Figure 3. A graphic display of the HardyVal Medium Risk Basic assessment. *This is an example procedure and does not necessarily reflect the procedure that every customer should use. Please refer to the guidelines detailed by your regulatory body to determine the best testing procedure for your laboratory.*

INTERPRETATION OF RESULTS

Visible growth or turbidity observed on or before 14 days of incubation is a positive test for the presence of bacteria. If positive, the media-fill challenge test has failed and indicates that a non-sterile technique was used during the test.

No visible growth or turbidity observed in 14 days indicates the media-fill challenge test was successful and the technique used during the media-fill challenge test was aseptic.

LIMITATIONS

Rare fastidious organisms may not grow in Tryptic Soy Broth.

Sterile empty vials may contain a small amount of sterile condensation. This will not affect the results of the test.

Refer to the document "[Limitations of Procedures and Warranty](#)" for more information.

MATERIALS REQUIRED BUT NOT PROVIDED

Standard supplies and equipment such as transfer tube sets, syringes, needles, adhesive seals, thermometers, incinerators, incubators, etc., as well as serological and biochemical reagents are not provided.

QUALITY CONTROL

Hardy Diagnostics tests each lot of commercially manufactured media using appropriate quality control microorganisms and quality specifications as outlined on the Certificates of Analysis (CofA). The following organisms are routinely used for testing at Hardy Diagnostics:

| Test Organisms | Inoculation Method* | Incubation | | | Results |
|--|---------------------|------------|-------------|------------|-------------------|
| | | Time | Temperature | Atmosphere | |
| <i>Bacillus subtilis</i> ATCC® 6633 | J | 1-3 days | 25-35°C | Aerobic | Growth; turbidity |
| <i>Candida albicans</i> ATCC® 10231 | J | 1-5 days | 25-35°C | Aerobic | Growth; turbidity |
| <i>Aspergillus brasiliensis</i> ATCC® 16404 | J | 1-5 days | 25-35°C | Aerobic | Growth; turbidity |

* Refer to the document "[Inoculation Procedures for Media QC](#)" for more information.

USER QUALITY CONTROL

End users of commercially prepared culture media should perform QC testing in accordance with applicable government regulatory agencies, and in compliance with accreditation requirements. Hardy Diagnostics recommends end users check for signs of contamination and deterioration and, if dictated by laboratory quality control procedures or regulation, perform quality control testing to demonstrate growth or a positive reaction and to demonstrate inhibition or a negative reaction, if applicable. Hardy Diagnostics quality control testing is documented on the certificates of analysis (CofA) available from Hardy Diagnostics [Certificates of Analysis](#) website. In addition, refer to the following document "[Finished Product Quality Control Procedures](#)," for more information on QC or see reference(s) for more specific information.

PHYSICAL APPEARANCE

Tryptic Soy Broth should appear clear, and light amber in color.

REFERENCES

1. *United States Pharmacopeia and National Formulary (USP-NF)*. Rockville, MD. United States Pharmacopeial Convention.

ATCC is a registered trademark of the American Type Culture Collection.

Whirl-Pak is a registered trademark of Nasco Industries, Inc.

HARDY DIAGNOSTICS

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The Hardy Diagnostics manufacturing facility and quality management system is certified to ISO 13485.

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Media-Fill Challenge

Log Sheet

Employee Name: _____ Employee Signature: _____ Date: _____

Evaluator Name: _____ Evaluator Signature: _____ Date: _____

Sample

| Cat. No. | | | | | | Lot: | | | | Exp Date: | |
|-------------|--------|---------|---------|----------|-----------------|----------|------------|-----------|-----------------|-----------------------|--------------------------|
| Vial Number | Hood # | Date IN | Time IN | Temp* IN | Lab Emp Initial | Date OUT | Time** OUT | Temp* OUT | Lab Emp Initial | Result (Growth - Y/N) | Pass / Fail ^t |
| Control 1 | | | | | | | | | | | P F |
| Control 2 | | | | | | | | | | | P F |
| Control 3 | | | | | | | | | | | P F |
| 1 | | | | | | | | | | | P F |
| 2 | | | | | | | | | | | P F |
| 3 | | | | | | | | | | | P F |
| 4 | | | | | | | | | | | P F |
| 5 | | | | | | | | | | | P F |
| 6 | | | | | | | | | | | P F |

*Required temperature of incubation is 30-35°C and/or 20-25°C per USP<797>.

**Required duration of incubation is at least 14 days

^tPass = No Growth(N), Fail = Growth (Y)

Supervisor Printed Name: _____

Supervisor Signature: _____

Date/time results acknowledged: _____