HardyVal™ CSP HIGH-RISK LEVEL MEDIA-FILL CHALLENGE TEST KIT

Cat. no. HVH1	High-Risk Level Media-Fill Challenge Test Kit	Single-Use Kit

Each kit contains:

Tryptic Soy Broth (TSB) Powder, 125ml Polycarbonate Bottle, 3gm Fill	1 bottle
Sterile 20ml Serum Vials (empty)	9 vials
Whirl-Pak® Bag	1 bag
Results Log Sheet	1 sheet

INTENDED USE

Hardy Diagnostics HardyVal™ CSP High-Risk Level Media-Fill Challenge Test Kit is recommended for routine use in the monitoring of aseptic procedures used in Compounding Sterile Preparations (CSPs). The kit contains the necessary materials for one pharmacist or technician to perform the semi-annual high-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 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 judgment and experience*.

Risk Level	Description	Examples	QA Monitoring and Frequency
Low	• 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.	• Single transfers of sterile dosage forms from ampules, bottles, bags, and vials using sterile syringes with sterile needles. *(Vancomycin 1gm in NS 100ml prepared for 1 patient.)* • Manually measuring and mixing no more than 3 manufactured products to compound drug admixtures and nutritional solutions. *(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.)*	**Media-Fill Challenge Test** *Low-risk Media-fill Challenge* Hardy Cat. no.: HVL1 Frequency: Annual testing for each person who compounds low-risk sterile preparations. **Environmental monitoring:** *Air Monitoring:* Hardy Cat. no.: G60 Frequency: At least semi-annual testing of each Laminar Air Flow Workbench or barrier isolator. *Surface and Glove Fingertips:* Hardy Cat. no.: P34 Frequency: 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.
Medium	• 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.	• 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. *(Chemotherapy prepared for infusion over 5 days using a portable infusion device.)* • 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. *(Implanted pump reservoir filled with Preservative-Free Morphine for infusion over 4 weeks.)* • Transfer from multiple ampules or vials into a single, final sterile container or product. *(Any IV solution compounded with more than 3 additives.)*	**Media-Fill Challenge Test** *Medium-risk Media-fill Challenge* Hardy Cat. no.: HVM1 and HVM2 Frequency: Annual testing for each person who compounds medium-risk sterile preparations. **Environmental Monitoring:** *Air Monitoring*: Hardy Cat. no.: G60 Frequency: At least semi-annual testing of each Laminar Air Flow Workbench or barrier isolator. *Surface and Glove Fingertips:* Hardy Cat. no.: P34 Frequency: 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.
High	• Non-sterile ingredients are incorporated or a non-sterile 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.	• Dissolving non-sterile bulk drug and nutrient powders to make solutions which will be terminally sterilized. *(TPN solutions made from dry amino acids.)* • Measuring and mixing sterile ingredients in non-sterile devices before sterilization is performed. *(Ophthalmic solution filtered into a non-sterile dropper bottle.)*	**Media-Fill Challenge Test** *High-risk Media-fill Challenge* Hardy Cat. no.: HVH1 Frequency: Semi-annual for each person who compounds high-risk sterile preparations. **Environmental:** *Air Monitoring*: Hardy Cat. no.: G60 and W28 Frequency: At least semi-annual testing of each Laminar Air Flow Workbench or barrier isolator. *Surface and Glove Fingertips:* Hardy Cat. no.: P34 Frequency: 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.

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 aseptic 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 high-risk level CSPs include all of the procedures for low-risk level CSPs. In addition, a media-fill test that represents high-risk compounding is performed semi-annually by each person authorized to compound high-risk level CSPs.

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 applies to the product in its intact packaging when stored as directed.

This product has the following shelf life from the date of manufacture:

Refer to the document "Storage" on the Hardy Diagnostics Technical Document website for more information.

PRECAUTIONS

This product may contain components of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not guarantee the absence of transmissible pathogenic agents. Therefore, it is recommended that these products be treated as potentially infectious, and handle observing the usual universal blood precautions. Do not ingest, inhale, or allow to come into contact with skin.

This product is for laboratory use only. It is to be used only by adequately trained and qualified laboratory personnel. Observe approved biohazard precautions and aseptic techniques. All laboratory specimens should be considered infectious and handled according to "standard precautions." The "Guidelines for Isolation Precautions" is available from the Centers for Disease Control and Prevention at www.cdc.gov/ncidod/dhqp/gl_isolation.html.

For additional information regarding specific precautions for the prevention of the transmission of all infectious agents from laboratory instruments and materials, and for recommendations for the management of exposure to infectious disease, refer to CLSI document M-29: *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline.*

Sterilize all biohazard waste before disposal.

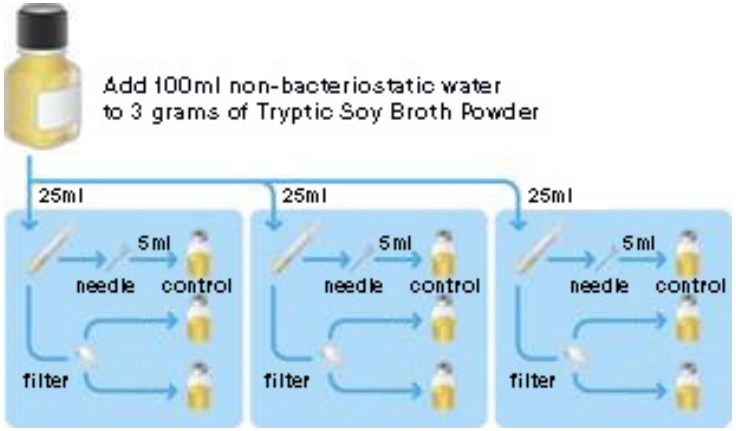
Refer to the document "Precautions When Using Media" on the Hardy Diagnostics Technical Document website for more information.

Refer to the document SDS Search instructions on the Hardy Diagnostics website for more information.

PROCEDURE

When performing media-fill risk challenges, use procedures and techniques that most closely resemble those used during routine compounding of High-Risk Level CSPs. If necessary, the following procedure may be modified to include more complex manipulations. Once begun, the test is completed without interruption. This procedure monitors aseptic technique and includes filtering a non-sterile solution through a micropore filter. "Controls" are included in the test procedure. Bacterial growth is expected in the "Control" vials because the solution dispensed into the vials is not sterile (contaminated) and has not been filtered.

1. Label the empty sterile 20ml vials with the date the challenge is performed and the initials of the person performing the procedure. Label three of the vials "**Control 1**", "**Control 2**" and "**Control 3**". Label the remaining six vials with the numbers "**1**" through "**6**".
2. In an area outside of the Laminar Air Flow workbench or isolator, remove the cap from the Tryptic Soy Broth powder bottle by unscrewing it. Using a graduated cylinder, prepare a 3% solution of non-sterile Tryptic Soy Broth by adding 100ml of water (non-bacteriostatic) to the bottle containing 3gm of powder. Replace the cap and tighten it. Invert the bottle several times to mix. Ensure that all of the powder is dissolved before proceeding.
3. Take the prepared non-sterile broth to the Laminar Air Flow workbench or isolator. Withdraw 25ml of the broth using a 30ml sterile syringe.
4. Transfer 5ml of the broth to the vial labeled as "Control 1".
5. Remove the needle from the syringe and using aseptic technique, affix a sterile 0.2 micron porosity filter unit and a 20-gauge needle to the syringe.
6. Inject 10ml from the syringe into the vial labeled "1". Inject another 10ml into the vial labeled "2".
7. Aseptically remove the filter unit and needle. Withdraw another 25ml of the non-sterile Tryptic Soy Broth. Transfer 5ml of the broth to the vial labeled as "Control 2".
8. Repeat steps 5 and 6 using vials "3" and "4".
9. Aseptically remove the filter unit and needle. Withdraw another 25ml of the non-sterile Tryptic Soy Broth. Transfer 5ml of the broth to the vial labeled as "Control 3".
10. Repeat steps 5 and 6 using vials labeled "5" and "6".
11. Aseptically apply sterile adhesive seals to the rubber closures of the nine vials.
12. Place all nine vials in a Whirl-Pak® bag for transport to the incubator.
13. Incubate the vials at 20 to 25 and/or 30 to 35°C for 14 days. If two temperatures of incubation are selected, incubate for 7 days at each temperature. Examine every few days for the presence of turbidity or growth of bacteria. ***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 used syringes, needles, filters and completed test vials as biomedical waste.



INTERPRETATION OF RESULTS

In the “Control” vials, the expected result is growth or turbidity because the medium was not sterile and was unfiltered.

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

No growth or turbidity observed in the vials containing filtered medium within 14 days, indicates the media-fill challenge test was successful and 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" on the Hardy Diagnostics Technical Document website for more information.

MATERIALS REQUIRED BUT NOT PROVIDED

Standard supplies and equipment such as syringes, needles, 0.2 micron filters, graduated cylinders, 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	
Bacillus subtilis ATCC® 6633	J	1-3 days	25-35°C	Aerobic	Growth; turbidity
Candida albicans ATCC® 10231	J	1-5 days	25-35°C	Aerobic	Growth; turbidity
Aspergillus brasiliensis ATCC® 16404	J	1-5 days	25-35°C	Aerobic	Growth; turbidity

* Refer to the document "Inoculation Procedures for Media QC" on the Hardy Diagnostics Technical Document website 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 documents on the Hardy Diagnostics Technical Document website for more information on QC: "Introduction to Quality Control" and "Finished Product Quality Control Procedures."

PHYSICAL APPEARANCE

Tryptic Soy Broth Powder should appear homogeneous, free-flowing, and light beige in color. The prepared media should appear clear and light amber in color. Empty sterile vials may contain a small amount of condensation.

REFERENCES

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

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

HDQA 2207H Rev. 012816hh

LOG SHEET
HIGH-RISK LEVEL MEDIA-FILL CHALLENGE

Name: _____ Date Test Performed: _____

Signature: _____ Kit Lot #: _____ Kit Expiration Date: _____

Vial Number	Hood Number	Incubation Temp.[1]	Length of Incubation[2]	Result: Growth/No growth	Interpretation: Pass/Fail	Notes/Corrective Action (Attach additional pages if necessary)
Control 1						
Control 2						
Control 3						
1						
2						
3						
4						
5						
6						

[1] Recommended incubation temperature is 20 to 25 and/or 30 to 35°C per USP <797>.
[2] Recommended length of incubation is 14 days for negative cultures.

_____
Supervisor Signature

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_____
Date

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