IFU

Instructions for Use

CSP ENVIRONMENTAL MONITORING AIR SAMPLING PLATES

Cat. no. G601	Tryptic Soy Agar (TSA), USP, 15x100mm Plate, 18ml	10 plates/bag
Cat. no. W28	Malt Extract Agar (MEA), 15x100mm Plate, 26ml	10 plates/bag

1 Results Log Sheet (included in this document)

INTENDED USE

Hardy Diagnostics Tryptic Soy Agar (TSA), USP and Malt Extract Agar (MEA) plates are recommended for use in compliance with routine monitoring of air quality required by USP Chapter <797> in areas used for compounding sterile preparations.

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 judgement and experience*.

Risk Level	Description	Examples	QA Monitoring
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.: G601 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 25º and 40ºC. *(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 Frequency: Annual testing for each person who compounds medium-risk sterile preparations. **Environmental Monitoring:** *Air Monitoring*: Hardy Cat. no.: G601 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 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.	• 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.: G601 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

Microbial contamination of sterile preparations can be caused by the quality of air in critical compounding areas. Assessment and verification of the adequacy and quality of the environment in which sterile preparations are compounded is essential. Evaluation of airborne microorganisms in the controlled air environments (Laminar Air Flow Workbenches (LAFW), barrier isolators, buffer or clean area and anteroom area) must be performed by trained individuals using electric air samplers and Tryptic Soy Agar (TSA) or Malt Extract Agar (MEA) plates. The use of settling plates for qualitative air sampling cannot be used to determine the air quality of a controlled environment. The area chosen for sampling should be done at areas most prone to contamination during compounding activities. This would include zones of air backwash turbulence within Laminar Air Flow Workbenches and other areas where air backwash turbulence may enter the compounding area. Sampling should also be conducted during activities such as staging, labeling, gowning, and cleaning. A sufficient volume of air should be tested at each location to maximize sensitivity. These evaluations are performed at periodic intervals, at least semi-annually as part of the recertification of facilities.

When using electric air samplers that actively collect volumes of air for evaluation, the devices must be validated. It is important that compounding personnel closely follow the air sampler manufacturer's recommended procedures. A sufficient volume of air (400 – 1000 liters) must be tested at each location in order to maximize sensitivity. The lids of the plates are removed and placed in the air sampler. Once the sampling cycle is complete, the plates are removed and the lids are replaced. The TSA plates are incubated at 30-35ºC up to 3 days for bacteria and 5 days for fungi. MEA plates are incubated at 26 +/- 2ºC for 5 to 7 days. The number of discrete colonies present on the surface of the media are counted and reported as Colony Forming Units (CFU). This provides a measurement of the level of microbial contamination in the air within the tested environment.

The formulation of Tryptic Soy Agar is prepared according to the United States Pharmacopeia (USP) standard formula for Soybean-Casein Digest Agar Medium.[3] It is also included in approved procedures in the *Compendium of Methods for the Microbiological Examination of Foods* and in *Standard Methods for the Examination of Water and Wastewater*.[1,2]

Tryptic Soy Agar contains digests of soybean meal and casein which provides amino acids and other nitrogenous compounds making it a nutritious medium for many microorganisms. Sodium chloride is added to maintain the osmotic equilibrium.

Malt Extract Agar, based on the formula recommended by Thom and Church, is designed to contain the proper formulation of carbon, protein and nutrient sources essential for yeast and mold growth. Dextrose is added to the medium to provide a carbon and energy source for fungi. Additionally, Malt Extract Agar contains digests of animal tissues (peptones) which provide a nutritious source of amino acids and nitrogenous compounds for the growth of mold and yeasts. The pH is adjusted to approximately 5.5 in order to enhance the growth of fungi and to slightly inhibit bacterial growth commonly found as environmental contaminants.

FORMULA

Ingredients per liter of deionized water:*

Tryptic Soy Agar:

Pancreatic Digest of Casein	15.0gm
Peptic Digest of Soybean Meal	5.0gm
Sodium Chloride	5.0gm
Agar	15.0gm

Final pH 7.3 +/- 0.2 at 25 degrees C.

Malt Extract Agar:

Malt Extract	20.0gm
Dextrose	20.0gm
Peptone	6.0gm
Agar	15.0gm

Final pH 5.5 +/- 0.3 at 25 degrees C.
*Adjusted and/or supplemented as required to meet performance criteria.

STORAGE AND SHELF LIFE

Storage: Upon receipt store at 2-8 degrees 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.

Refer to the document "Storage" for more information.

PRECAUTIONS

For laboratory use only. 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

Consult manufacturer's user manual for instructions on operating the electric air sampling device.

All risk levels must sample each location using a Tryptic Soy Agar (TSA) plate to detect bacterial contamination. For high risk level compounding a Malt Extract Agar (MEA) plate shall be used to test the same location (in a separate sampling cycle) in order to detect fungal or mold contamination.

1. Position the sampler at least 6 inches inside the work area and at one end of the Laminar Air Flow Workbench (LAFW) or barrier isolator. Using a new plate, repeat the air sampling cycle at the other end of the LAFW. (If the LAFW or isolator is located in a "cleanroom", sample another area outside of the LAFW. A location inside the cleanroom but near the entrance is preferred.)
2. Carefully remove the lid of the plate and place the plate containing agar in the air sampling device.
3. When the sample cycle is complete, carefully replace the lid of the plate, remove the plate and incubate at 30-35 degrees C. for up to 3 days for bacteria and 5 days for fungi. MEA plates should be incubated for 5 to 7 days at 28 +/- 2 degrees C.
4. Count the number of discrete colonies present and report as Colony Forming Units (CFUs) per cubic meter of air.

INTERPRETATION OF RESULTS

Table 4. Recommended Action Levels (Counts) of Microbial Colony-Forming Units (cfu) per Cubic Meter of Air or Contact Plate

ISO Class of Sampled Location	**Sampled Sources and Their Action Levels (Counts) of Microbial CFU[a]**		
	Active Air[b]	**Glove Fingertip**	**Surface Sample (contact plate) (cfu per plate)**
5	**>1**	**>3**	**>3**
7	>10	Not applicable	>5
8	>100	Not applicable	>100

[a] The CFU action levels are obtained from USP <797>.

[b] At least one cubic meter (m^3) or 1000 liters (L) of air must be sampled.

Because of the inherent variability of environmental sampling methods, it is more useful to trend contamination recovery results rather than to focus on the number of colonies recovered from a particular sample. Action should be required when the contamination recovery rate trends above the recommended action levels for a significant time.

If action levels have been identified, a thorough investigation into operational procedures, cleaning procedures and air filtration efficiency within the compounding area must be made. Once changes have been made, monitoring procedures should be repeated to determine if the changes made were effective. Documentation of all air monitoring results, remedial action and follow-up monitoring must be maintained. The Results Log Sheet, included in this document, may be used for this purpose.

LIMITATIONS

Growth of rare fastidious organisms may not be supported on Tryptic Soy Agar or Malt Extract Agar.

Refer to the document "Limitations of Procedures and Warranty" for more information.

MATERIALS REQUIRED BUT NOT PROVIDED

Standard microbiological supplies and equipment such as counting devices, thermometers, incinerators, incubators, etc., as well as serological and biochemical reagents are not provided.

QUALITY CONTROL

The following organisms are routinely used for testing at Hardy Diagnostics:

Test Organisms	Inoculation Method*	Incubation			Results
		Time	Temperature	Atmosphere	
Tryptic Soy Agar:					
Candida albicans ATCC® 10231	J	1-5 days	30-35ºC	Aerobic	Growth
Bacillus subtilis ATCC® 6633	J	1-3 days	30-35ºC	Aerobic	Growth
Staphylococcus aureus ATCC ® 6538	J	1-3 days	30-35ºC	Aerobic	Growth
Pseudomonas aeruginosa ATCC ® 9027	J	1-3 days	30-35ºC	Aerobic	Growth
Aspergillus brasiliensis ATCC ® 16404	J	1-5 days	30-35ºC	Aerobic	Growth
Malt Extract Agar:					
Aspergillus brasiliensis ATCC ® 16404	G	2-7 days	15-30ºC	Aerobic	Growth
Candida albicans ATCC® 10231	A	24-48hr	15-30ºC	Aerobic	Growth
Saccharomyces cerevisiae ATCC® 9763	A	24-48hr	15-30ºC	Aerobic	Growth

USER QUALITY CONTROL

Check for signs of contamination and deterioration. Users of commercially prepared media may be required to perform quality control testing with at least one known organism to demonstrate growth or a positive reaction; and at least one organism to demonstrate inhibition or a negative reaction (where applicable). Also, see listed references for more information.

PHYSICAL APPEARANCE

- Tryptic Soy Agar, USP should appear translucent, and light amber in color.

- Malt Extract Agar should appear clear, slightly opalescent, and light to medium amber in color.

REFERENCES

1. American Public Health Association. 2012. *Standard Methods for the Examination of Water and Wastewater*, 22nd ed. APHA, Washington, D.C.

2. APHA Technical Committee on Microbiological Methods for Foods. 2001. *Compendium of Methods for the Microbiological Examination of Foods*, 4th ed. APHA, Washington, D.C.

3. The Official Compendia of Standards. *USP-NF*. United States Pharmacopeial Convention, Rockville, MD.

4. USP General Chapter <797> Pharmaceutical Compounding, Sterile Preparations. United States Pharmacopeial Convention Inc., Rockville, MD.

5. U.S. Food and Drug Administration. *Bacteriological Analytical Manual*, AOAC, Arlington, VA. http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm2006949.htm

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LOG SHEET
CSP ENVIRONMENTAL MONITORING

Date Tested	Workbench #	Area Tested	By	Routine (R) Remedial (X)	# of CFU/cubic meter of air	Comments: (Acceptable or Corrective Action Taken)	Supervisor

Remove lid of plate and place plate in air sampler. Select cycle on air sample. When cycle is complete, re-cover and then incubate plates per USP Chapter <797>.