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the pure observer

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Incubation and Analysis of USP <797> Microbiology Samples: Do We Keep It In-house or Outsource?

The USP <797> changes to viable sampling, gloved fingertip and thumb testing, and media-fill testing frequencies have left many sterile compounding organizations asking if they should incubate and analyze these samples or outsource to a contract lab. Making this decision is more involved than just figuring out where you will put the incubators. If you are trying to determine what is right for your organization, you must take a hard look at your operations and facility. There is one question that you must answer honestly before even starting to research what it will take to incubate and analyze samples.

Are we willing to hold our sterile compounding organization accountable to the same standards as an accredited contract microbiology lab?

If the answer is no, ask why? Think about other services you outsource. Maybe you purchase preparations from 503B Outsourcing Facilities. You likely hold those providers to a certain level of excellence. If you had to prepare those medications in-house, you'd have a certain internal standard that needed to be met. How is this different from sample incubation and analysis? It's not. Keeping incubation and analysis in-house, without meeting microbiology lab best practices, is a huge risk to the integrity of your results and the safety of your patients. If you decide this is not for your organization, it's time to research contract microbiology labs that specialize in the processing of USP <797> samples.

If the answer is yes, your sterile compounding organization is on its way to also becoming a microbiology lab. Here are some questions to ask to help determine if you are ready to bring incubation and analysis in-house.

1. Have you read USP <1117> Microbiological Best Laboratory Practices, and do you understand what is required to be a lab?

   This informational chapter discusses everything you will need to consider in meeting the minimum expectations of operating a lab, such as training, equipment use and maintenance, and lab layout. This chapter is only available in the full compendium. If your organization only has the compounding compendium, it does not have access to this valuable chapter.

2. Do we have a dedicated space for incubation and analysis?

   Incubators cannot be in the cleanroom suite or in the perimeter of the segregated compounding area (SCA). Best practice is to have either a room or dedicated area in the general pharmacy for incubation and analysis. If it is in the general pharmacy, choose a low-traffic area away from areas where people may be eating or drinking. The worksurface (counter or table) where samples will be analyzed should not be a desk or an area where staff eat or keep drinks.

best practice makes perfect.

Thoroughly read the manufacturer's use instructions for your incubators. Many incubators require back and side clearance to ensure proper function. The instructions for use will also include preventive maintenance considerations.

3. Do we have at least two incubators, one at 30-35 °C and one at 20-25 °C, with calibrated temperature monitoring devices?

   USP <797> requires that viable air, surface, and gloved fingertip and thumb samples and media-fill tests be incubated in an incubator. Although the chapter does not indicate that the temperature of the incubator cannot be changed, changing incubator temperature is not recommended for a few reasons.

   - The incubator monitoring device will need to be calibrated at two temperatures. Although the chapter does require that the temperature monitoring devices be calibrated, this is best practice and would need to be calibrated initially and at least every 12 months if not defined by the manufacturer.
   - When incubating media-fill tests and gloved fingertip and thumb and surface samples at the same time, it is not recommended to leave the gloved fingertip and thumb and surface samples in the 30-35 °C incubator for 7 days until the media-fill test finishes its first incubation. This extended incubation at the warmer temperature could dry out the media and result in recovered colonies not being viable for identification.
   - There is a risk that staff will forget to change the temperature on the incubator for the next incubation.
   - You will not be able to start incubation of any 30-35 °C samples if the incubator is set at 20-25 °C.

4. Are the incubators lab-grade with a digital display?

   High-quality incubators are a significant initial investment, but they are worth it. The incubators are going to get a lot of use and you want them to last for many years. Having a digital display will make setting the temperature so much easier than having an analog dial.

5. Is the temperature in the incubator monitored?

   Temperature monitoring can be done a few ways. It could be monitored by simply checking a calibrated thermometer daily and documenting the temperature. The issue with this method is that, if there were a temperature excursion between readings, you would never know. Monitoring could be done with a calibrated chart recorder, which does allow you to see excursions between temperature checks. Ideally, the temperature is monitored through a continuous monitoring device. Temperature readings can be taken every few minutes. This provides the most robust incubator monitoring and is the choice of many contract labs. Just be prepared for temperature excursion notifications at 2 AM.

6. Are the incubators qualified?

   Incubator qualification is essential to ensure the incubators work as expected. It has three main components:

   - Installation – Is the incubator installed properly?
   - Operation – Does the incubator operate as expected?
   - Performance – How does the incubator operate under different scenarios?

   The qualification will include temperature mapping, looking for hot and cold spots in the incubator. It will also usually include power-off and open-door studies. These provide invaluable data in the event of temperature excursions. The full qualification is performed initially, and aspects of the performance qualification should be repeated annually or biannually, based on your equipment maintenance SOP.

7. Is there an SOP on how to handle incubator temperature excursions?

   Temperature excursion will happen. You must define what is a temperature excursion and draft an SOP on how the organization will handle the excursion. Someone on staff must be able to assess how the temperature excursion affected the test samples and this assessment must be documented.

8. Is there a preventative maintenance plan in place for the incubators?

   Check the user manual for suggested preventative maintenance. This could include:

   - Verifying incubator clearance at the top, sides, and back
   - Adjusting the feet so the door swings closed
   - Checking the cord integrity
   - Cleaning the interior and exterior of the incubator

9. Are the incubators on a generator or back-up power supply?

   This is critical. The best way to prepare for handling a power loss-related excursion is to do a power-off study as part of the initial performance qualification.

10. Do we have staff with the appropriate background to be analyzing samples?

    USP <1117> indicates that "the demands of microbiological testing require that the core educational background of the staff, supervisors, and managers be in microbiology or a closely related biological science. They should be assigned responsibilities in keeping with their level of skill and experience." Remember, if you sent samples out to a contract microbiology lab, you would expect staff to be adequately trained and experienced. You need to expect the same of your staff. Your staff might not have a background in microbiology. This makes it all the more critical to form a relationship with a microbiologist or contract lab that can assist you with challenging situations. You must get adequate training for your staff who will be analyzing samples.

11. Are staff trained to count colony forming units and analyze media-fill tests?

    Not all of your samples are going to have 2 or 3 colonies, making training in sample analysis nonnegotiable. A microbiology lab would have an extensive training program for sample analysis. It could take a new lab trainee weeks to be signed off counting colonies; and, even after being signed off, they are likely to need some assistance in determining how many colonies might actually be present. A new lab trainee's training could include:

    - Learning about the different colony morphologies they are likely to encounter
    - Taking a written exam on the different colony morphologies
    - Observing a trained individual counting colonies a defined number of times
    - Counting practice samples until the trainer feels the trainee is ready to be tested
    - Taking a practical test on counting colonies

    Reading media-fill tests requires knowledge of different microbial growth patterns in broth and the ability to determine if a media-fill sample has growth in a container-closure system that is not clear. Subculturing from the final media-fill container may be necessary. Staff must have training on how to do this.

12. Do staff have time to dedicate to the analysis of samples?

    In a contract lab, sample analysis is the lab staffs' primary responsibility. This is likely not true in a sterile compounding facility, resulting in the reading of samples being rushed or pushed off until there is time. The timely reading of samples is critical to taking action in the event of an excursion of a failed competency assessment.

13. Do we have a way to properly dispose of used media?

    There must be a way to properly dispose of test samples. Contact your waste disposal provider to identify the local and state requirements.

14. Are there SOPs in place for how to count colonies and analyze media-fill tests?

    There must be SOPs defining the procedures for analyzing test samples. The SOP would include things like preparing the work area, donning appropriate personal protective equipment (PPE), analyzing the sample, documenting the result, reporting excursions to the appropriate individuals, preparing samples for identification by the contract lab, and reporting data.

15. Do we have a separation of operations and the quality entity?

    In a contract lab, the individuals who perform the testing and sample analysis are not the same individuals who review the testing for compliance with established SOPs and standards. There is a clear separation of operations from the quality entity. Sterile compounding organizations incubating their own samples must have a way to ensure the ethical testing and reporting of microbiological data.

    If you answered no to any of these questions, you need to assess the gap, identify remediation options, and implement the appropriate corrective actions. With the expected focus from surveyors and inspectors on viable sample collection and sample analysis, sterile compounding facilities must be prepared to defend their decision to keep sampling, incubation, and analysis in-house.

USP <797> doesn't define an order. Consider putting the mask on first and the beard cover over top. This keeps the beard cover from scrunching up and ending up in the person's mouth.

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puremicrobiology.com
E: abby@puremicrobiology.com | P: 610.417.4795

Abby Roth, founder of Pure Microbiology, has been supporting the testing and consulting needs of the pharmaceutical, medical device, and compounding industries since 2004. Her background in pharmaceutical microbiology includes extensive knowledge of environmental monitoring. Abby also has participated in multiple microbial excursion investigations, providing guidance on contamination sources and remediation options.