Getting It Under Control: Products and Procedures for Environmental Monitoring

Photo courtesy of Hardy Diagnostics

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PROGRESS: THE CONCEPT THAT INDIVIDUALS AND THE PROFESSION HAVE moved forward and improved, based on a steady increase of knowledge and wisdom that comes from challenges. Since USP Chapter <797> was published two years ago, pharmacists and technicians have been working hard to meet the challenges of the chapter and to improve their sterile compounding operations. Currently, <797> requires only air sampling as part of an environmental monitoring program. Specifically, it is required once monthly for low- and medium-risk level compounding operations, and once weekly for high-risk compounding operations.

A well-designed environmental monitoring program will demonstrate that the engineering controls, disinfection practices, employees, and compounding processes are capable of consistently maintaining acceptable levels of microbials. The program should be capable of detecting adverse trends in microbial populations and facilitate the identification of its source, be it equipment failure, sanitization practices, personnel habits, or training deficiencies, so they may be corrected before the environment or the product is adversely affected.

Types of Sampling

There are three types of environmental monitoring metrics: air, surface, and personnel. Although <797> only requires air sampling at this time, the value of personnel and surface testing should be considered. It is a direct indication of appropriate or inappropriate material handling, cleaning practices, gowning, and personnel habits.

Routine personnel monitoring should be conducted. Gloves should be sampled both before changing them and at the completion of the process. Personnel should gently touch the agar surface of the plates with their gloves, at which point the gloves must be changed or disposed.

Contact plates, swabs, or paddles are some of the tools you can use to sample your surfaces. Surface sampling is intended to recover microbials present on surfaces that could be introduced into your final compounded sterile preparations. After any type of surface sampling, areas need to be cleaned with isopropyl alcohol or another suitable agent to remove any media residue.

Passive, gravity, depositional, or settling sampling is a non-quantitative collection method in which an agar medium is exposed to the environment and airborne organisms are collected primarily by gravity. Active sampling is a quantitative method in which an electric air sampler is set to draw in a known volume of air and transfer microbials to an agar surface. Passive air sampling has been thought to give the pharmacist a qualitative indication of what biologically active particles (BAPs) may actually fall into compounded sterile preparations. It was assumed that BAPs will settle on the agar plate, in the same manner that they would in the compounded sterile preparation.

We now have a greater understanding of the limits of passive air sampling. Collection of airborne microorganisms by this method is affected by the size and shape of the particles and by the motion of the surrounding air. As a result, large particles are more likely to be deposited on the collection surface, leading to a misrepresentation of the prevalence of airborne microorganisms and the exclusion of smaller particles from collection. In addition, the concentration of the airborne microorganisms cannot be determined by gravity sampling, because the volume of air from which the particles originate is unknown. Settling plates do not measure the number of microorganisms in the air; rather they measure the number of microorganisms settling from the air onto a known surface area in a known time.[1] Gravity sampling has been compared to various methods that pass a known volume of air to the collection medium. The results show that the airborne concentrations derived from gravity sampling are not qualitatively or quantitatively accurate and do not compare favorably with those obtained by other methods, such as active sampling.

Active sampling is a quantitative means of sampling air and by far the most accurate for measuring the amount of biologically active particles (BAPs).[2] Since a known quantity of air is sampled, the pharmacist can easily determine the concentration of BAPs in the compounding environment and compare that result to previous results. This allows the pharmacist to detect increases in BAPs and take actions to decrease the population to acceptable levels.

Product Selection

The key to a successful environmental monitoring program lies in the selection of appropriate tools. Consideration must be given to the availability of the components, cost, ease of use, expiry dating, and storage requirements.

Selecting an Air Sampler

There are a variety of air samplers available for use, the two most commonly used technologies in this industry are impaction and centrifugal force. Since the purchase of the electric air sampler (new or used) will likely be the most expensive part of the environmental monitoring program it is important to choose one that is suitable for your program for the lowest cost. The following should be considered during the selection process:

Disruption of Air Flow: It is vital that the flow of air in critical environments is not disrupted by the air sampler. This is most often encountered when purchasing older equipment.

Flow Rate: The sampler should have a flow rate high enough to sample the required volume of air without drying out the media.

Volume: The sampler should be equipped with a volume selector.

Media: Is the media needed for the sampler readily available? Can the media be used to sample other areas or is it specific to that sampler?

Physical Aspects: The sampler should be portable, easily disinfected or autoclaved, sturdy, and manageable. Tricky manipulations for placing media in the sampler will increase the risk of contamination by the operator.

Calibration: Calibration services should be readily available. What is the turn-around time for calibration?

Cost to maintain: The unit should be easily maintained and cost-effective.

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Photo courtesy of Biotest

Selection of surface/personnel sampling equipment:

	ADVANTAGES	DISADVANTAGES
Swabs	Good for use in sampling switches and irregular surfaces. May be purchased with a neutralizer incorporated into the media	Requires additional manipulations and equipment to obtain quantitative results
Contact plates	May be directly incubated. May be purchased with a neutralizer incorporated into the media. Same media used for some electric air samplers and personnel sampling	Agar surface may become disrupted when sampling irregular surfaces
Contact paddles	May be directly incubated. Good for hard to reach places	Does not have a neutralizer incorporated into the media

Selection of Media

Media generally falls into one of three categories: general growth, selective, and differential. Specialized agar may be incorporated into environments where a particular type of organism may cause concern, or where certain organisms may not be detected because of the growth of other organisms. For most applications though, a general growth medium is sufficient as it will support the growth of a large variety of organisms, including bacteria, yeast, and mold. A chemical neutralizer must be incorporated into the surface sampling media to neutralize any cleaning product residues left behind, which may inhibit growth. Be sure the product you choose is capable of neutralizing the type of cleaning chemicals you use. Media for air samples do not generally require the incorporation of neutralizers, unless you use a gas decontamination method, such as vaporized hydrogen peroxide in an aseptic contamination isolator.

A Certificate of Analysis (C of A) or Certificate of Performance should be provided by the manufacturer for each lot of media received by your facility, and should be reviewed and filed by the pharmacists.

Sample Processing, Microbial Evaluation, and Data Analysis

There are several factors that need to be considered when processing environmental samples and evaluating the data. One consideration should be incubation parameters. Most bacteria will grow at 30°C to 35°C in 48 to 72 hours, while most molds are visible at three to five days at 20°C to 25°C. Dual incubation will afford the opportunity to recover more microbials and obtain a more reliable evaluation of the environment.

The extent of microbial evaluation also needs to be determined. Your evaluation of the data needs to provide enough information to show trends and facilitate an investigation. It is critical that the data be routinely reviewed and used as a means to identify problems before they happen. Acting on upward trends is critical. These changes give you an indication when the facility or process is moving away from a state of control. Shifts or increases in the number of CFUs often occur prior to a process or facility failure.

On the other hand, collecting too much data can be overwhelming and unmanageable. Speciation (the identification of the microorganism) may be helpful on critical product contact areas, but a basic breakdown of bacteria into groups is usually sufficient for other areas.

An alert level may not necessarily require action; however, it may be prudent to prevent an action level. Action levels will stimulate an investigation, and all required actions described in your protocol should be followed. Depending upon the number and type of organisms recovered, the investigation may include activities surrounding gowning, training, material handling, and aseptic technique. At a minimum, the compounding area should be cleaned and re-sampled to show that desired levels have been reestablished. At the conclusion of the investigation, any preventable causes or suggested changes should be investigated and, if warranted, incorporated into future procedures to prevent reoccurrence.

Summary

Understanding environmental monitoring will provide you with valuable information about the state of control of your compounding operation. This objective data will allow for the investigation and remediation of problems before they affect the quality of the final compounded sterile preparation. To ensure the quality of your compounded preparations, it is vital that you invest the upfront time to create the appropriate procedures for your environmental monitoring program. These procedures must be matched with the proper products to ensure success. P&P

References

Hurst CJ, *Manual of Environmental Microbiology, ed. 2*, 2002, American Society of Microbiology (ASM) Press, Washington, DC.

Mosley, GA, Hanson, M: Microbial Monitoring of Controlled Environments and Alert and Action Limits, *Controlled Environments Magazine*, June 2004

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Where to find it:

VENDOR	READER SERVICE #
Becton, Dickinson and Company	91
bioMerieux	14
Biotest Diagnostics	16
Bioscience International	19
Hardy Diagnostics	20
Millipore Corporation	89
Q.I. Medical, Inc.	88
Remel	86
Veltek Associates Inc.	85

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