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Board of Registration in Pharmacy

Advisory: Media Fill Testing

Based on recommendations from the Advisory Committee to the Board of Registration in Pharmacy ("Board"), guidance has been developed regarding the media fill testing process in sterile compounding pharmacies. Media fill testing (also known as process simulation) is one aspect of competency testing of sterile compounding personnel. This advisory is designed to provide additional guidance for conducting media fill tests to supplement the requirements of USP <797>.

I. Purpose

The current 2008 version of USP <797> defines a media fill test as "a test used to qualify aseptic technique of compounding personnel or processes and to ensure that the processes used are able to produce sterile products without microbial contamination. During this test, a microbiological growth medium such as soybean–casein digest medium is substituted for the actual drug product to simulate admixture compounding."

Media fill tests are one of many qualitative indicators to aid in the evaluation of aseptic technique to assure the quality and safety of compounded sterile products ("CSPs"). The results of media fill testing can also be used for the training of compounding personnel as well as providing valuable insight into the compounding environment, workflow procedures, and any equipment used in compounding.

II. Procedural Considerations

A. Policies and Procedures

Develop policies and procedures to encompass the full media fill test procedure from set-up to completion including, but not limited to:

i. media selection and list of any needed equipment / supplies

ii. criteria established in advance of media fill (e.g., type of simulation, number of personnel present, time(s) of day, indicators of failure, etc.)
iii. instructions and / or master formulation record (e.g., non-sterile to sterile compounding)
iv. incubation and monitoring of filled units
v. method(s) of documentation for tracking media fill tests, results, and trends for each individual
vi. corrective action process for any identified media fill failures

Additionally, sterile compounding pharmacies should have a written change control process to evaluate the impact of any changes or events that have the potential to affect the sterile compounding process and that may require additional (or different) media fill tests.

B. Testing Conditions

USP <797> (2021 revised draft) states "when performing a media-fill test, simulate the most difficult and challenging compounding procedures and processing conditions encountered by the person replacing all the components used in the CSPs with soybean–casein digest media."

Simulate sterile compounding utilizing the facility's commonly used container closure systems (e.g., bags, vials, etc.) and processes:

i. with the greatest number of manipulations (e.g., parenteral nutrition, etc.);
ii. with longest fill time;
iii. utilizing any compounding equipment; and / or
iv. involving any specialized procedures (e.g., use of closed-system transfer devices, filtration sterilization, etc.).

Additional factors to consider when simulating the most challenging processing conditions are the maximum number of personnel typically present and the time of day (e.g., end of shift, times of greatest compounding activity, etc.).

C. Number of Tests and Frequency Recommendations

i. Initial qualification:
    a. three (3) media fill tests should be completed, each followed by gloved fingertip/thumb sampling

ii. Ongoing qualification (each followed by gloved fingertip/thumb sampling):

a. at least one media fill test every six (6) months if prepare CSPs using only conventionally manufactured sterile starting components; or
b. at least one media fill test every three (3) months if prepare CSPs using any non-sterile starting components.

iii. Additional testing:

a. for media fill test failures, repeat initial qualification procedure
b. following significant changes (e.g., new equipment, etc.)
c. part of a root cause analysis ("RCA") (e.g., defective drug product, etc.)

D. Media Considerations

In addition to verifying the growth promotion capability as outlined in USP <797>, check the expiration date of the media and document it along with the lot number.

E. Incubation

Incubate the final media fill containers for 14 days at the temperature ranges specified by USP and / or media manufacturer's recommendations. Monitor the temperatures either manually or by a continuous recording device. Temperatures should be reviewed and documented at least daily on the days the pharmacy is open.

F. Inspection of Filled Units

It is recommended that completed media fill test containers be examined at least every 2 - 3 days or in accordance with manufacturer recommendations.

If incubating the filled units "in-house", it is recommended that the results are monitored by an individual other than the individual who performed the test to assure independent monitoring.

III. Interpretation of Results

In addition to visible turbidity (cloudiness) or other visual manifestations ("strings" or "clumps"), media fill failures can also be indicated by color changes in the media, particle generation, or gas production.

Inadvertent vial cores in the media indicates poor compounding technique and may be difficult to distinguish from microbial growth. In either case, requalification is indicated for the individual.

In the case of a media fill failure, it is important not to shake the units as it may interfere with a potential microbiological analysis (i.e., aerobic organisms on top, anaerobic organisms at the bottom).

Discard results if it is suspected that the failure is due to causes such as container closure failure, media contamination, or incubator temperature excursion rather than compounding personnel failure.

IV. Corrective Action / Follow-up

In the event an individual fails a media fill test, they may not compound until retrained and requalified.

Evaluate any potential impact to sterile compounds previously prepared by an individual who has failed a media fill test.

In the event of repeated or multiple failures (i.e., multiple persons; same person / multiple failures), the media fill units should be sent out to a qualified laboratory for identification / speciation. These results may be helpful to identify the causes of the failure especially when considered with other personnel or environmental monitoring results.

Maintain all documentation of media fill testing including results and any corrective actions.

Please direct any questions to: **Pharmacy.Admin@mass.gov**

References

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