NEWSLETTER ISSUE: JANUARY 2025

the pure observer

Stay current on compounding, contamination control, and compliance best practices with pure microbiology

Controls for USP <797> Viable Samples

Controls for USP <797> viable samples have been a hot topic recently. Let's answer some common questions about the use of controls.

Does USP <797> require controls to be used?

No. The chapter does not mention the use of controls for any type of viable samples or tests (air, surface, gloved fingertip and thumb, or media fill).

Will the lab require the use of controls?

Maybe. Each lab will have specific recommendations for using controls for viable sample collection.

Is the use of controls a best practice?

Yes. Viable sample collection for USP <797> more closely resembles viable sample collection for GMP manufacturing facilities than it does indoor air quality (IAQ) sampling. Controls are used for many different tests in the CGMP world and are a strongly recommended best practice.

Which industry documents suggest the use of controls?

The Controlled Environment Testing Association (CETA) Application Guide (CAG)-009 titled Viable Environmental Monitoring for Sterile Compounding Facilities has a section dedicated to the use of controls and describes the use for both negative and positive controls.

The Parenteral Drug Association (PDA) Technical Report 13 (TR13) titled Fundamentals of an Environmental Monitoring Program discusses the need to "justify and document the quality control strategy for media used for

environmental monitoring, including the need to perform sterility checks and negative controls." This is what you'd expect from a GMP-based document. Do a risk assessment and figure it out based on your facility.

USP <1117> Microbiological Best Laboratory Practices discusses how some microbiological methods described in the USP require the use of a negative control and suggests that "their use in other situations should be relevant and appropriate." Handling media devices during a viable sampling session seems like a situation where a negative control would be "relevant and appropriate," doesn't it?

What are the different types of controls according to CAG-009?

Negative control: Media device(s), per lot of media used in sampling, that is removed from the manufacturer's packaging but is not opened. This is done to simulate device handling during sample collection. The negative control is kept with the test samples from collection through incubation. The control is acceptable if no microorganisms are recovered after incubation.

Positive control: Media device(s) that is unopened and sent to the microbiology lab to be inoculated with <100 colony forming units (CFUs) of different microorganisms for a growth/no growth test (also known as growth support testing). This is NOT the same as collecting a super dirty sample from the floor or the sole of someone's shoe (yuck!). We are trying to show that the media can recover specific microorganisms. See USP <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests for more information on specific cultures.

- *Staphylococcus aureus* → Gram positive cocci
- *Pseudomonas paraeruginosa* → Gram negative rod
- *Bacillus subtilis* → Spore-forming rod
- *Candida albicans* → Yeast
- *Aspergillus brasiliensis* → Mold

All the microorganisms inoculated on the positive control must grow before the shortest incubation period ends. For example, the first incubation period for USP <797> tryptic soy agar (TSA) samples is least 48 hours at 30 to 35 °C. The lab would inoculate the control with bacteria, yeast, and mold. All the bacteria

inoculated on the control must grow BEFORE the 48-hour mark for the media to be considered acceptable. If the yeast and mold did not grow out in this time (although they likely would), the control would be transferred to 20 to 25 °C for no more than 5 days to allow the fungal organisms to grow.

How many of each control do I need?

This is not discussed in CAG-009. Your lab can provide guidance. As a best practice, consider 2 of each type of control used. Having two of each control can be useful in the event of a control failure.

How do I decide if I need controls?

For viable air and surface sampling, a negative control is a must every time—without exception. For the positive control, this decision really comes down to whether the microbiology lab you use can perform proper positive control testing. And even if they can do the testing, they might charge for it. So, the recommendation is as follows:

Certification company or pharmacy that outsources incubation	Submit	Rationale
If the lab provides growth support testing at no charge…	Negative control Positive control	If it's included, always do it.
If the lab provides growth support testing for a charge and samples are shipped overnight…	Negative control Positive control	Shipping comes with risk. It's worth the money.
If the lab provides growth support testing for a charge and samples are dropped off at the lab the next day…	Negative control Positive control	Storing samples comes with risk. It's worth the money.
If the lab provides growth support testing for a charge and samples are dropped off at the lab the same day…	Negative control	There is no storage or shipping of samples. Less risk.

Pharmacy with in-house incubation	Incubate	Rationale
If the pharmacy incubates samples at each location or at a centralized location…	Negative control	The pharmacy does not have the ability to properly perform growth support.

What happens if there is a control failure?

Negative control: There are a variety of factors that must be considered in determining whether the samples were truly compromised. For example, if the negative control has growth, but all the other samples had 0 CFU, the lot of media itself was not likely the issue and plate handling should be investigated. You would not throw out the data from this sampling set. If the growth on the negative control was also seen throughout the sample set, either the lot itself was somehow contaminated or there was a plate handling issue. In either case, the sampling session should be repeated and an investigation is needed.

Positive: If the positive control does not support growth, the lab must confirm that the control was inoculated. If it was and lab error is ruled out, the lab can try setting up another positive control with a sample that did not have growth at the end of incubation. If the positive control still does not support growth, quarantine the media lot, contact the manufacturer, and repeat the sampling session with a different lot of media.

Need more guidance? Pure Microbiology can help. Contact us for more details!

best practice makes perfect

Verify that your SCA really is clean, uncluttered, and dedicated to compounding. Many times, there is a lot of activity in and around the SCA resulting in piles of papers and stacks of boxes.

QUESTION of the MONTH

Can we perform our own USP <71> Sterility Testing?

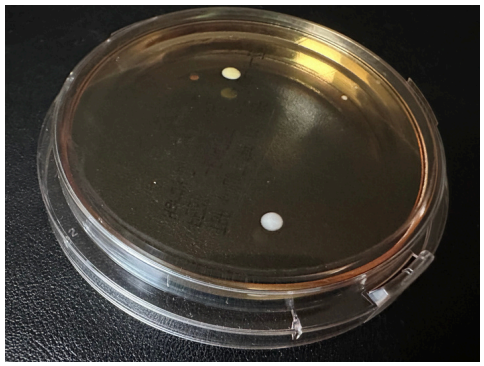
Although there is nothing in USP <797> stopping you from doing this, it is not recommended. Sterility testing is a compendial release test that comes with significant responsibility and microbiology lab capabilities, like having and using cultures of microorganisms for method suitability testing. Leave it to the experts.

Colony Enumeration Proficiency Assessment

Pure Proficiency's Colony Enumeration Proficiency Assessment is a state-of-the-art proficiency test that provides an in-hand assessment without the use of live microbial samples. It gives you the third-party documentation you need to demonstrate proficiency in counting colonies.

Now available for purchase on the Pure Microbiology website!

Order your kit today!



Join Us For

Pure Primer
Sterile Compounding and Handling Hazardous Drugs

June 2-5, 2025
November 10-13, 2025
Bethlehem, PA

Join us for a 3.5-day in-person training, including lectures and skill-building activities. Two and a half days are spent focusing on USP General Chapter <797> requirements, best practices, and implementation strategies, while one day emphasizes the importance of USP General Chapter <800>, exploring requirements and real-life solutions. This interactive training is appropriate for both pharmacists and technicians, especially those who hold a management or designated person role.

Attendees will receive 25.5 hours of live ACPE CE.

Instructors include:
Abby Roth, CMQ/OE
Patricia Kienle, RPh, MPA, BCSCP, FASHP
Kevin Hansen, PharmD, MS, BCSCP
Lew Exner

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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.