An Inside Look at USP <71> Webinar Q&A

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1. **How is the amount of volume to be tested for method suitability determined? If for example, we make 150 x 10mL vials and have a method suitability performed on this volume, but next time we make 250 vials, would this be covered under our first method suitability, based on Table 3?**

   Method suitability validates the ability of a sterility test method to recover all 6 microorganisms. Method suitability volume is based on performing the sterility test procedure multiple times. A filtration sample requires 3 times the sterility testing volume for method suitability. The total sample volume is split 50/50 between two sample media. Each of the 6 organisms uses half the sample volume. The organisms are added separately to the appropriate media.

   6 Organisms x ½ Test Volume Each = 3x Test Volume

   Example: A pharmacy needs to validate a 100 mL sample volume.

   6 organisms x 50 mL each = 300 mL

   Pharmacists should refer to USP <71> Table 3 to check USP requirements when making different batch sizes. Table 3 is used to determine the minimum number of articles (finished product) to be tested in relation to number of articles in a batch.

   150 vials falls into the "More than 100 containers, but not more than 500 containers" category, as does a 250 vial batch. For any batch size between 100 and 500, 10 vials must be tested. Method suitability does not need to be repeated since the same volume (10 x 10 mL = 100 mL) satisfies the testing requirements.

2. **Is it a requirement to potency test each batch if a BUD study is done or can we do every other batch or whatever we decide?**

   Routine potency testing of release batches is necessary to evaluate product quality. While a BUD study is extremely important to establish dating, it does not provide assurance that regular production batches are compounded correctly.

3. **If the sample is not greater than 1 mL why do you need to double the qty? How is it then sampled? In the presentation 28 mLs were sampled of the 36 provided.**

   The quantity is doubled to meet the requirements of Tables 2 & 3.

   Table 2 *Minimum Quantity to be Used for Each Medium*, states if a container is < 1 mL, the whole contents of each container is used for each media. If the fill is between 1-40 mL, pharmacists must test a minimum 1 mL per media. Media requires at least 1 mL each. There are two media; therefore, the quantity needs to be doubled requiring 2mL.

   Sidenote:

   In Table 3 *Minimum Number of Articles to be Tested in Relation to the Number of Articles in the Batch,* the right column is "Minimum Number of Items to be Tested for Each Medium". If the contents of one container are enough to inoculate the two media, the right column in Table 3 gives the number of containers needed in both the media together.

   If the contents of one container (e.g. 1mL) are NOT enough to inoculate the two media (as described in Table 2) then to meet the volume requirements to be tested in Table 2, the article requirement from Table 3 must be doubled (e.g. 2mL).

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4. **For method suitability testing, would the largest batch max out at the greatest number needed to run a 71 test?**

   Yes, for a given formulation, pharmacists should perform method suitability based on the largest potential batch.

   For example, a batch of more than 500 containers requires 2% or 20 containers, whichever is less to be submitted. A pharmacy could perform method suitability based on a 20 article submission to cover any future, larger batch size.

   An important caveat to this is the container fill volume must remain the same or smaller. If twenty 10 mL vials from a 500+ article batch are submitted for testing, the volume to test equals 200 mL. If the container is changed to a 20 mL vial, a total of 400 mL will be tested (20 x 20mL). If method suitability was performed based on a 200 mL submission, method suitability needs to be repeated to cover the 400 mL volume.

5. **Can media fills be left on the pharmacy counter, temperature range - room temperature? Must media fills be incubated at a constant temperature?**

   USP <797> states requirements for temperature control for the incubation of media fills. Media Fills should be maintained at the specified controlled temperature(s) for the full 14 day incubation period as outlined in USP <797>.

6. **What is the importance of closure integrity of a container with respect to method suitability? E.g. Does switching container size or container type, require a new method suitability analysis?**

   The container and closure should not affect method suitability. The formulation is the critical factor in method suitability. As long as the formulation and volume remains the same, a change in container does not require a new method suitability procedure.

7. **Will fungi grow in the short incubation time 3-5 days? Testing batches for fungi is 14 days enough time?**

   The 5-day incubation period is used for growth promotion and method suitability of the two fungal organisms, *Aspergillus brasiliensis and Candida albicans*. The organisms should show visual growth by the Day 5 evaluation if the media is capable of growing the organisms. The 14-day incubation sterility test is based on providing an adequate period for both bacterial and fungal organisms to grow.

8. **How would you test for mold or spores?**

   The Trypticase soy broth (TSB), one of the two required media for USP <71> testing, should recover yeasts, molds, and fungal spores. The TSB media's ability to recover fungi is verified in the growth promotion test with the two fungal organisms. Bacterial spores will germinate in either the FTG or TSB media, depending on the organism.

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