Submitting Samples for Sterility Testing

The following information is to be used only as a guideline for submitting samples and is not intended to replace any requirements listed under USP <71>, USP <795>, and USP <797>, nor is this to be used as an interpretation of USP guidelines. **THE CLIENT IS RESPONSIBLE FOR ENSURING COMPLIANCE WITH USP GUIDELINES.** Please refer to USP <795> and <797> for good compounding practices, and your State Board of Pharmacy for other requirements.

I. Sterility by USP <71>

In order to list USP <71> as the test method ARL **must** be able to trace method suitability data to your specific formulation. This can be accomplished in 2 ways:

1. Method Suitability Library Verification
2. Method Suitability Validation

Please allow two weeks for the completion of the method suitability validation of each new formula, and three business days for the method suitability library verification of each new formula.

ARL can evaluate your formulation in advance of you submitting samples for testing, just provide the information requested below.

Method Suitability Library Verification

Please provide a copy of the formulation sheet in order to perform a method suitability library verification. If we already have method suitability data that applies to a formulation, we can reference that data instead of repeating the testing. ARL refers to this process as method suitability library verification. The formula sheet should contain a listing of all actives/excipients and have a unique formulation identification number assigned by your pharmacy. If the formulation sheet contains a sub-formula this must be submitted as well. Please include the package insert for any commercial products used in the formulation. We require formulations to be exactly the same in order to have the same formulation ID number.

If you cannot/will not provide a formulation sheet ARL will not be able to do a method suitability library verification and will need to perform a Method Suitability Validation (see below).

Please note: ARL maintains confidentiality and does not share information about our clients or their specific formulations. We can provide a non-disclosure agreement if desired.

In summary ARL requires:

1. Formulation sheet with unique formulation identification number
2. Formulation sheets for any sub-formulas
3. Package insert for any commercial products used in the formulation
4. Information on the largest amount of sample you plan to have tested (consider # of articles and container volume)

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Method Suitability Validation

Method suitability is a process by which samples are inoculated with the six organisms listed in USP <71>. If clearly visible growth of all microorganisms is obtained after incubation, visually comparable to a control, the method is suitable as a sterility test for the formulation.

This one time test is required if we cannot reference existing data via our method suitability library verification or if you do not/cannot submit a formulation sheet. Once we have a passing method suitability on a particular formula, we do not need to perform the test again unless the formula changes or there is a required change in the testing method i.e., increase in the number of articles or article volume.

If method suitability does not pass using the original test method it will need to be repeated and additional sample will be required both for another method suitability test as well as any sample testing setup using the original method.

In summary ARL requires:

1. A unique formulation identification number (formulation sheet is desired but not required)
2. Three times the largest amount of sample you plan to have tested (consider # of articles and container volume)
    a. For example, if 100 mL was the most sample you would need tested (i.e., 10 vials with 10 mL each) then we would need 300 mL to perform the method suitability validation

We recommend performing method suitability on the formula containing the highest possible concentrations of the actives/preservatives and with the largest volume that you anticipate needing to have tested. That method suitability will cover batches made from a similar formula with lower concentrations of actives or in lower volumes. Method suitability will be required if the concentrations/volumes are higher.

ARL prefers clients to submit a formulation sheet for method suitability validation but this is not required. A unique formulation ID number is required as this is how we will trace the method suitability data to your specific formulation.

Please provide three times the largest amount of sample you anticipate will need to be tested. If you have a limited supply of product, please call to discuss.

Sampling for Testing

In order for ARL to list USP <71> as the test method the correct number of articles must be submitted in accordance with Table 3 in the chapter. (Note: Table 2 also applies to containers with <2 mL. If containers have <2 mL, please double the number of containers to send and certify that number.) Containers with greater than 100 mL are considered a large volume parenteral. When samples are submitted you must sign certifying that you have sent in the proper number of articles according to USP <71>. If you do not/cannot sample per USP <71> ARL will list our internal sterility method, MBI-144, as the test method.

II. Sterility by MBI-144

MBI-144 Sterility method is designed to capture a broad range of contaminating microorganisms including aerobic, anaerobic, and spore forming bacteria as well as fungal microorganisms, including yeasts and molds. MBI-144 sterility test are performed according to USP <71> guidelines with respect to the media used for testing, incubation temperatures and incubation times. The test preparations are observed for macroscopic evidence of microbial growth and at the end of the incubation period (14 or 18 days) a "Sterile" result is released which indicates that the product being examined complies with the test for sterility and no contaminating microorganism has been found in the sample.

This is an internal ARL method that will be cited in the event that you do not provide the proper number of articles per USP <71> or method suitability cannot be traced to your specific formulation. This method does not fully comply with USP <71> for these reasons. We will choose the sterility test method based on our current method suitability library using the product description. In the event that there is no method suitability data matching the sample description, i.e. no indication of the appropriate test method for sterility, method suitability validation will be required. Please see the above section on method suitability testing/verification requirements above.

III. Sending in the samples for testing

Please complete our on-line Sample Submission Form (www.arlokapps.com). It is important that you certify the number of containers being sent for USP <71> sterility testing and submit the formulation ID number. If applicable, please identify on the submission form what articles are for method suitability testing and which articles are for additional tests that you have requested. You can also complete our manual submission form which can be obtained from our web site www.arlok.com. Please enclose a copy of the submission form with your samples.

Unique Formulation ID Number (Required for testing by USP <71>)

The unique formulation identification number (from the formulation sheet or that you generate) must be submitted each time a sample made from that formula is sent for sterility testing. This same ID can be used for the same formulation in different packages. For example, if a batch of testosterone in oil was produced and then packaged into 5 mL vials, 10 mL vials and 5 ml syringes, each package would be sent in for testing as a separate batch (different container/closures need to be treated as different batches) but the formulation ID submitted for the testosterone formulation could be the same for all three. ARL will use this number to definitively show that method suitability data is traceable to your specific formulation (either by method suitability library verification or method suitability validation as described above). Please be aware that the unique formulation ID number is case sensitive in our database so it is important the submission form includes the exact formulation ID number.

Requesting sterility by USP <71> without providing a formulation ID number for the formulation will result in a requirement for additional sample(s) to be provided for method suitability testing, and your facility may experience delays in reporting of results. The best way to prevent delays on testing of a new formulation is to ensure that you have provided not only the formulation sheet with a unique formulation ID number, but also additional sample that may be required for method suitability testing (please reference the section on Method Suitability Validation).

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Incomplete or missing information on submission forms will delay testing. Our staff will make attempts to notify you if additional information is required. Please let us know the name of the person to contact, and the preferred method of contact, i.e. e-mail or phone.

In the event that you are sending in additional sample for testing as requested by ARL after the original submission of the sample; it is extremely important to reference the original ARL number in order to prevent confusion and/or delays.

Please send separate containers for each additional test being ordered, such as potency, endotoxin, and fungal. If you certify that a certain number of articles are required to meet USP <71> batch size requirements, then we must use all of those articles when performing the test. Please call if your finished product article is less than 2 mL or greater than 50 mL. We cannot share containers between the Microbiology Lab and our other labs.

IV. Reporting of Sterility Results

We will strive to provide your sterility test results to you as soon as possible. However, please keep in mind that the incubation process cannot be rushed. Depending on the time of day that your sterility test begins incubation, your result may not be ready until the evening of the sterility read date. We will release a preliminary report after 72 hours (or 3 business days) of incubation. The final report will be released after 14 or 18 days of incubation, whichever is appropriate for your sample.

Please call at 800-393-1595 if you have any questions.

Thank you, Debbie Hunt
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