Rapid Sterility FAQs

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About the Celsis® ATP-bioluminescence Method

1. How does the Celsis system work, and why is it better than competing technologies?

The Celsis Rapid Sterility Method is a growth-based sterility test, which detects microbial contamination based on the presence of microbial Adenosine triphosphate (ATP) in a sample. Because it is a growth-based test, it can be more readily compared to the compendial USP <71> test used for decades. Additionally, when comparing it to other competing technologies, the Celsis Rapid Sterility test allows for the processing of multiple sample types (solutions, oils, suspensions, etc.), and because it does not require filtration of the test media, microbial identification can be performed in the event of a test failure.

2. Is the method validated?

Yes, it has been validated by the vendor (Charles River), by numerous labs around the world, and at ARL. Our validation strategy is based on direction given in USP <1223> Validation of Alternative Microbiological Methods. Our final validation report is available upon client request.

3. What is the sensitivity of the test, and how was it determined?

During validation testing, the Celsis Rapid Sterility test demonstrated non-inferiority to the USP <71> test using very low (<1 CFU) inoculum counts. The Limit of Detection (LOD) testing was based on direction defined in USP <1223> Validation of Alternative Microbiological Methods.

4. What controls are put in place to ensure an accurate result?

Daily positive and negative controls are tested during each shift, which assess the equipment's functionality to ensure all aspects of the assay are working appropriately. Additionally, internal quality control parameters are defined to ensure consistency in reported data.

5. Does 797 allow for the use of rapid sterility?

Yes; USP <797> states that, when required, sterility testing "must be performed according to <71> or a validated alternative method that is non-inferior to <71> testing". Chapter <1223> is referenced for the validation of alternative microbiological methods.

6. Is the method acceptable to FDA?

Yes; product validations using the Celsis system have been approved by regulatory agencies worldwide, including the FDA.

Method Suitability

1. Is method suitability required?

As with any thorough sterility test, yes, method suitability is required to ensure a proper method is chosen to assess each unique product formulation.

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Method Suitability (continued)

2. Does method suitability need to be performed again if I already have one on file for <71>?

Yes, since it is a unique test, new method suitability testing must be performed.

3. Are Library References allowed?

A method verification will be offered in some cases. This can be considered a "partial" method suitability test. Briefly, the sterility test method of a similar product formulation can be referenced if rapid sterility method suitability is on file. ARL will perform a sample effects assessment on the new product formulation to confirm that the method referenced does not interfere with the Celsis assay.

4. What is the test volume required for method suitability?

ARL requires 4x sterility test volume to complete method suitability.

3x the sterility volume is used for inhibition testing (similar to USP <71> method suitability testing), and an additional full sterility test volume is used for sample effects testing, which ensures the product formulation does not interfere with the Celsis Rapid Sterility assay itself.

5. If my batch size increases, will I have to re-perform Method Suitability?

Generally, yes. Most methods are volume-dependent, which means an increase in sterility test volume will need to be re-evaluated to determine an appropriate test method.

Sample Submission and Results

1. What is the price?

- Rapid Sterility: $250
- Rapid Sterility for Antimicrobial Active and Metered Devices: $350
- Method Suitability: $995
- Method Suitability for Antimicrobial Active and Metered Devices: $1,750
- Method Verification: $750

2. What is the turnaround time?

Rapid Sterility test has a 6 calender day turnaround time with samples set up on the day of arrival.
Rapid Sterility test has a 8 calendar day turnaround time for metered devices.
Method suitability has a 10 business day turnaround time.

3. How much sample is required for the sterility test?

ARL suggests submission of the full USP <71> required test volume. These recommendations are made based on statistical likelihoods of detecting a contaminant in a batch, should one be present.

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Sample Submission and Results (continued)

4. Will the test method be cited as USP <71>?

No, USP <71> is written clearly to state that samples are to be incubated for a minimum of 14 days. ARL's validation testing was performed to thoroughly assess the specificity and Limit of Detection of the technology, where we ultimately deemed to be non-inferior to the compendial sterility test.

5. What is the Rapid Sterility OOS Investigation Procedure?

If a Rapid Sterility test result indicates growth may be present, the sample is then listed as "Under Investigation" and the media canisters will be placed back into the incubators for one business day. If visual growth is observed after one additional business day of incubation, the sample status will be updated to "Not Sterile" and the out of specification (OOS) investigation will proceed. If no visual growth is observed following the additional incubation, invalidation of the initial result is possible with two additional rapid sterility retests of the original sample where no growth is detected. The additional rapid sterility reads carry a $200 fee, which will be waived if the original result is invalidated **(CLIENT APPROVAL REQUIRED)**. If growth is detected in the duplicate retests, the sample status will be updated to "Not Sterile" and the OOS investigation will proceed.

6. If I fail sterility with rapid, can I retest with <71> and release my batch if <71> passes?

ARL does not tell a client whether they should release a batch after any failed sterility test results. A full investigation should be performed assessing the failing result, after which a decision regarding batch release is made by the client.

7. Are there formulations that ARL's Rapid Sterility Platform cannot test?

The number of formulations unable to be tested by rapid sterility is very low. Certain formulations contain properties which interfere with the ATP Luciferase reaction utilized by the Celsis Rapid Sterility method. This precludes them from being tested using this platform.