
celsis®
RAPID MICROBIAL DETECTION

ABOUT THE SPEAKER

Jonathan Kallay
Senior Director of Technology and Market Development

Jonathan (Jon) Kallay is a Senior Technical & Market Development Manager working remotely for the Microbial Solutions product lines. He is a subject matter expert on microbiological investigations for manufacturing facilities that make regulated products. Jon provides practical laboratory experience to help clients identify the optimal path forward for their labs.

Jon received his Bachelor's degree in biochemistry from Denison University before earning a post-graduate diploma in pharmaceutical microbiology from the University of Manchester.


celsis®
RAPID MICROBIAL DETECTION

Sterility Test Flow *with Celsis*

Sterility Testing

Same day Transfer

Incubation

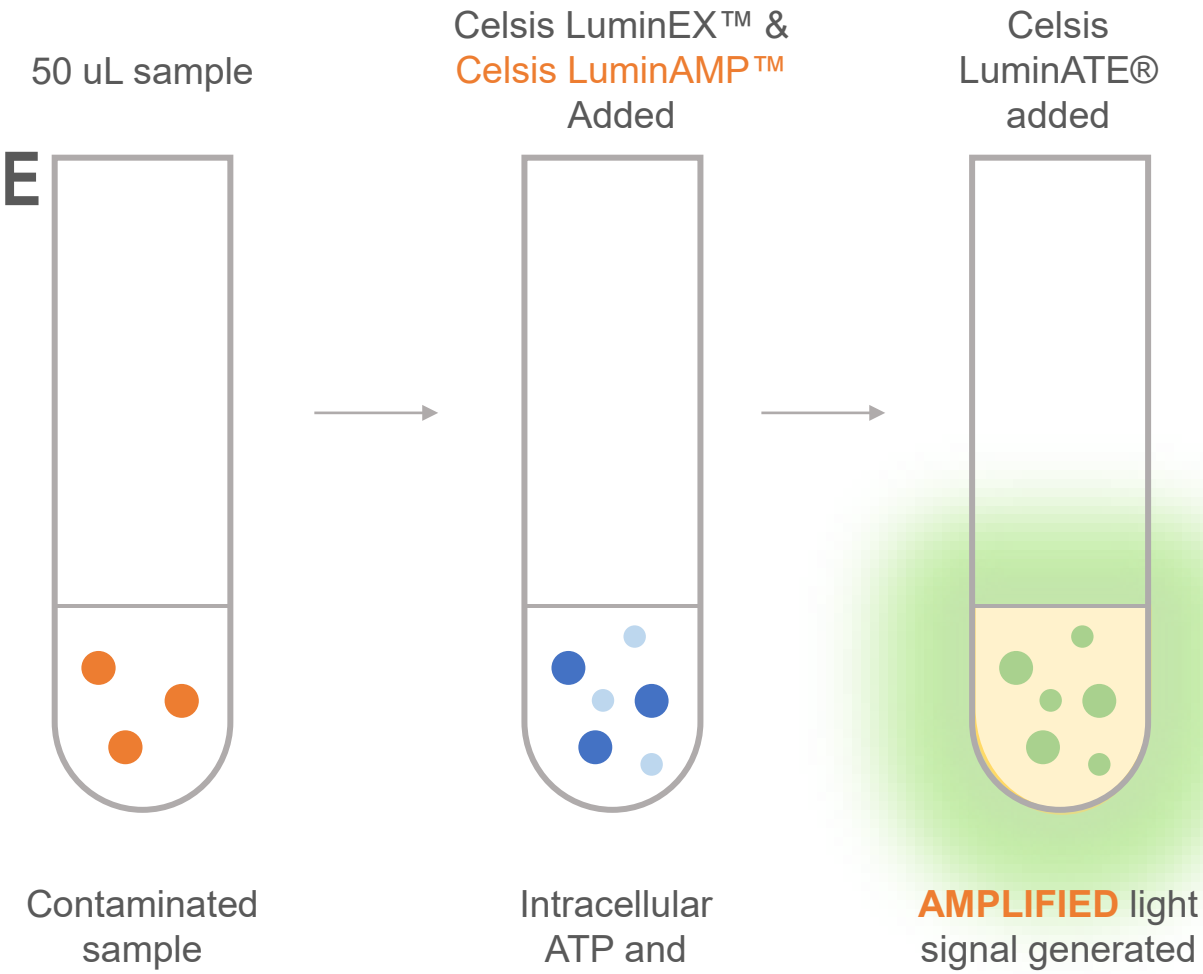
14 Day Incubation

Reading Results

CELSIS AMPISCREEN® AMPLIFIED ATP BIOLUMINESCENCE

Celsis® ATP-Bioluminescence Reagents

- Two-phase, proprietary enzyme reaction
- All living organisms also contain the enzyme adenylate kinase (AK) as part of their biochemical processes
- Microbial enzymes convert ADP into ATP
- Amplification of ATP levels beyond naturally occurring level.
- Enzymes are not depleted by reaction
- Ability to generate almost unlimited amounts of ATP



the Celsis Accel®
Product Code: 7460288

Complete RMM Solutions.

What does yours look like?

the Celsis Advance II™
Product Code: 7456004

Celsis AMPiScreen® Pharma Reagent Kit

400 Assay Reagent Kit
Product Code: RST400

Sartorius Sterisart® NF for Celsis®

Celsis® Qualified Sterisart® NF Septum with 4 cm dual-needle
Product Code: 16466CR-GSD

Celsis® Qualified Sterisart® NF Septum with 5.2 cm needle
Product Code: 16467CR-GSD

Hardy Diagnostics Media for Celsis®

Celsis® Qualified Hardy Diagnostics Tryptic Soy Broth, USP, 100 mL Septum Top Glass Vial
Product Code: CM1010

Celsis® Qualified Hardy Diagnostics Fluid Thioglycollate Medium, USP, 100 mL Septum Top Glass Vial
Product Code: CM1015

Charles River Implementation and Validation Support

Celsis® Complete Validation & Reports

Method Validation documentation for Equivalency, Specificity, Robustness, Ruggedness, and Limit of Detection. cGMP Validation Testing in Presence of Product for Method Suitability, Equivalency, Limit of Detection, Specificity.
Product Code: VAL6000MF

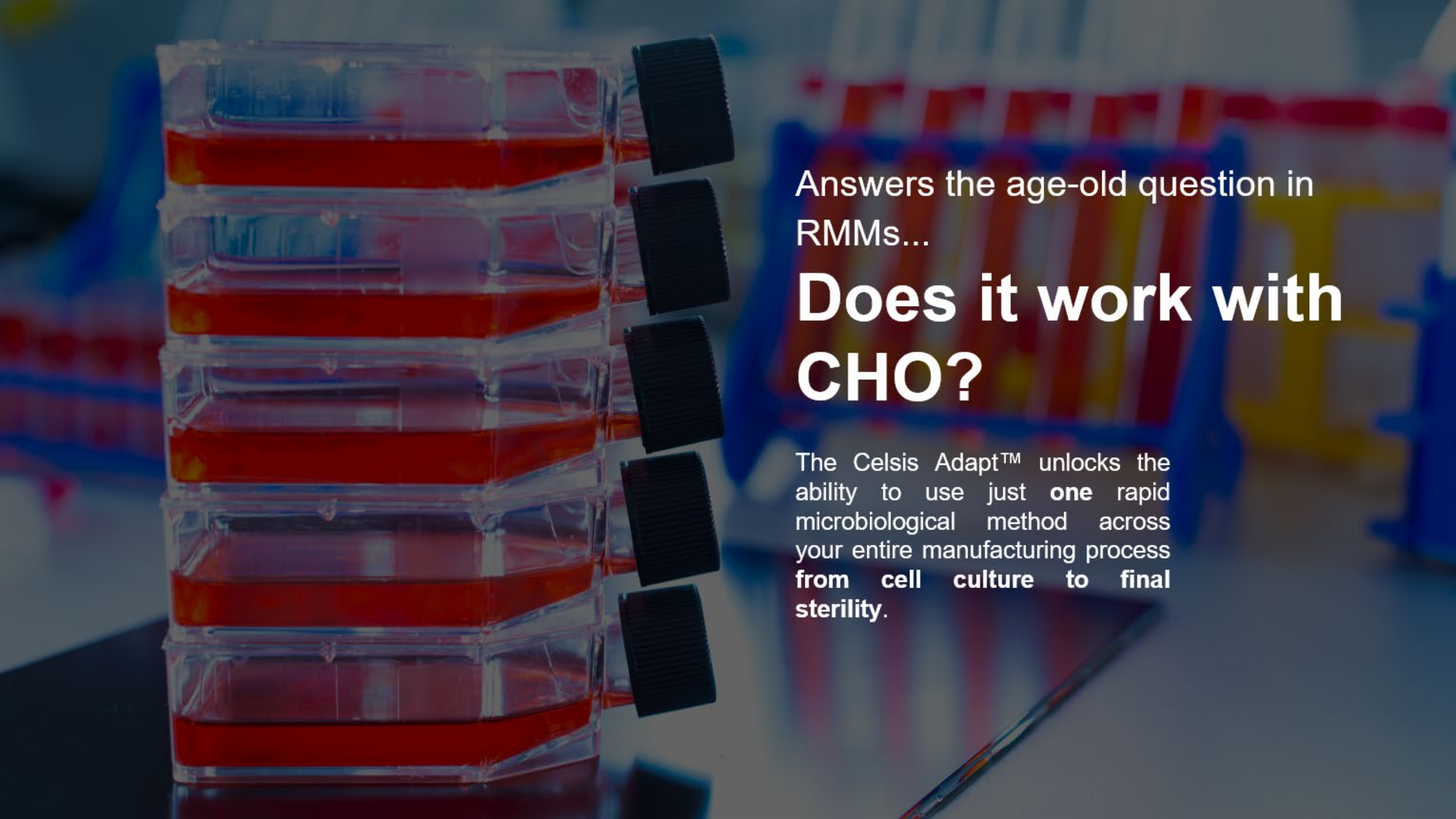
Celsis® Advantage Reports & Protocols

Method Validation documentation for Equivalency, Specificity, Robustness, Ruggedness, and Limit of Detection. Protocols for Testing in Presence of Product for Method Suitability, Equivalency, Limit of Detection, Specificity.
Product Code: VAL6100MF

Installation Support and Ongoing Training

Celsis® 3 Day Initial Installation and Training
Product Code: TS0003

Celsis® 1 Day Supplemental Training
Product Code: TS0001



Answers the age-old question in RMMs...

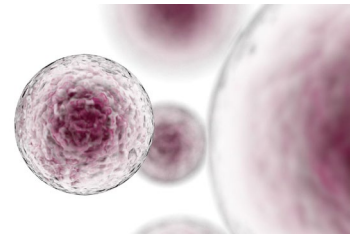
Does it work with CHO?

The Celsis Adapt™ unlocks the ability to use just **one** rapid microbiological method across your entire manufacturing process **from cell culture to final sterility**.

CELSIS ADAPT

Celsis Adapt™ Introduction

Demonstrated detection of broad range of microorganisms, **including fungi.**

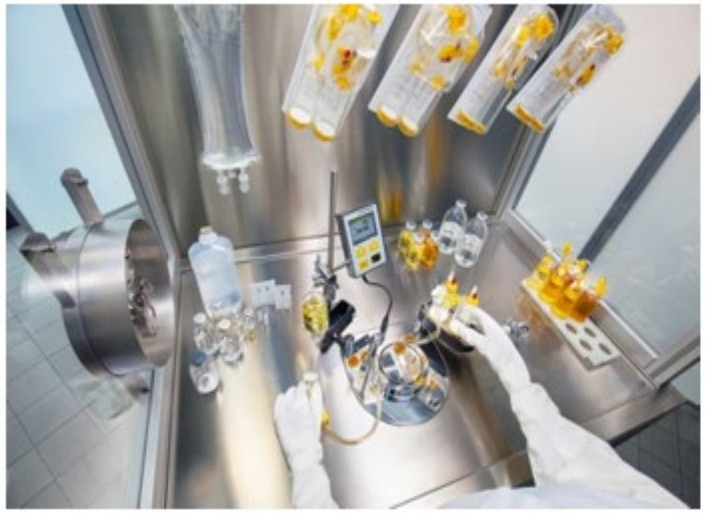


Compatible with various cell lines used in bioprocessing of pharmaceuticals and cell & gene therapies.

Aligns with current and new regulatory requirements for the use of alternative rapid microbiological methods.

Sterility Test Flow *With Celsis Adapt*

Sterility Testing



Same day Transfer

Incubation

Product Cell Removal

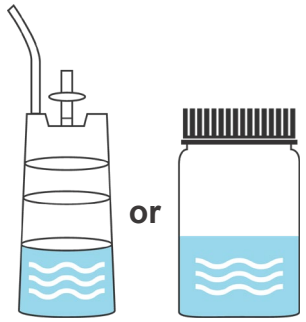
6 Day Incubation

Reading Results

Same day Testing

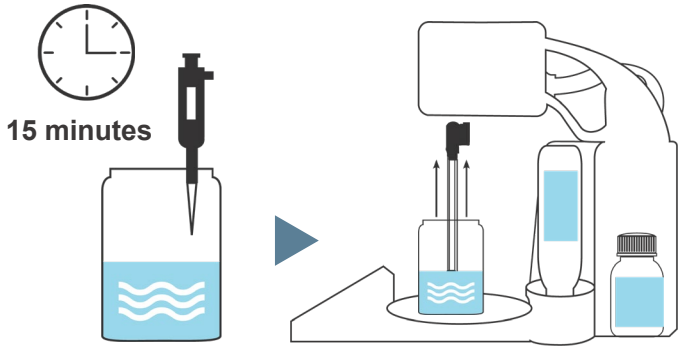
CELSIS ADAPT™ PREP PROCESS OVERVIEW

Celsis Adapt™ Methodology & Workflow



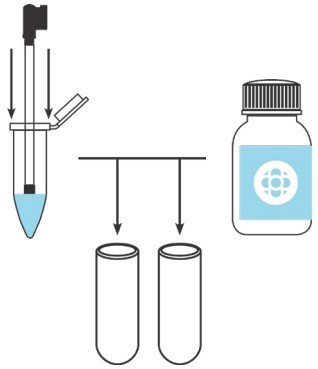
Prepare & Incubate

- **Prepare sample using compendial method** TSB/FTM media used
- **Incubate for 3-7 days**



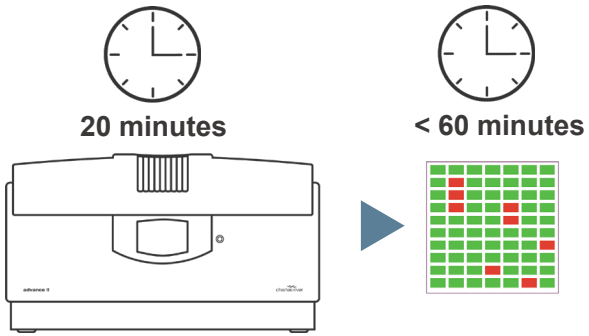
Lyse & Concentrate

- Aseptically **remove sample aliquot and** add to **Treatment Solution**
- Allow for a minimum **dwell time of 15 minutes**
- **Concentrate** using Adapt™



Pipette Concentrate + Celsis LuminASE®

- Combine aliquot of **concentrate and reagent** to sterile assay cuvettes.



Run on Celsis® instrument

- **Load samples** into Celsis Advance II™
- Allow **20-minute ATP depletion step**
- **Obtain rapid qualitative results** reported in positive or negative

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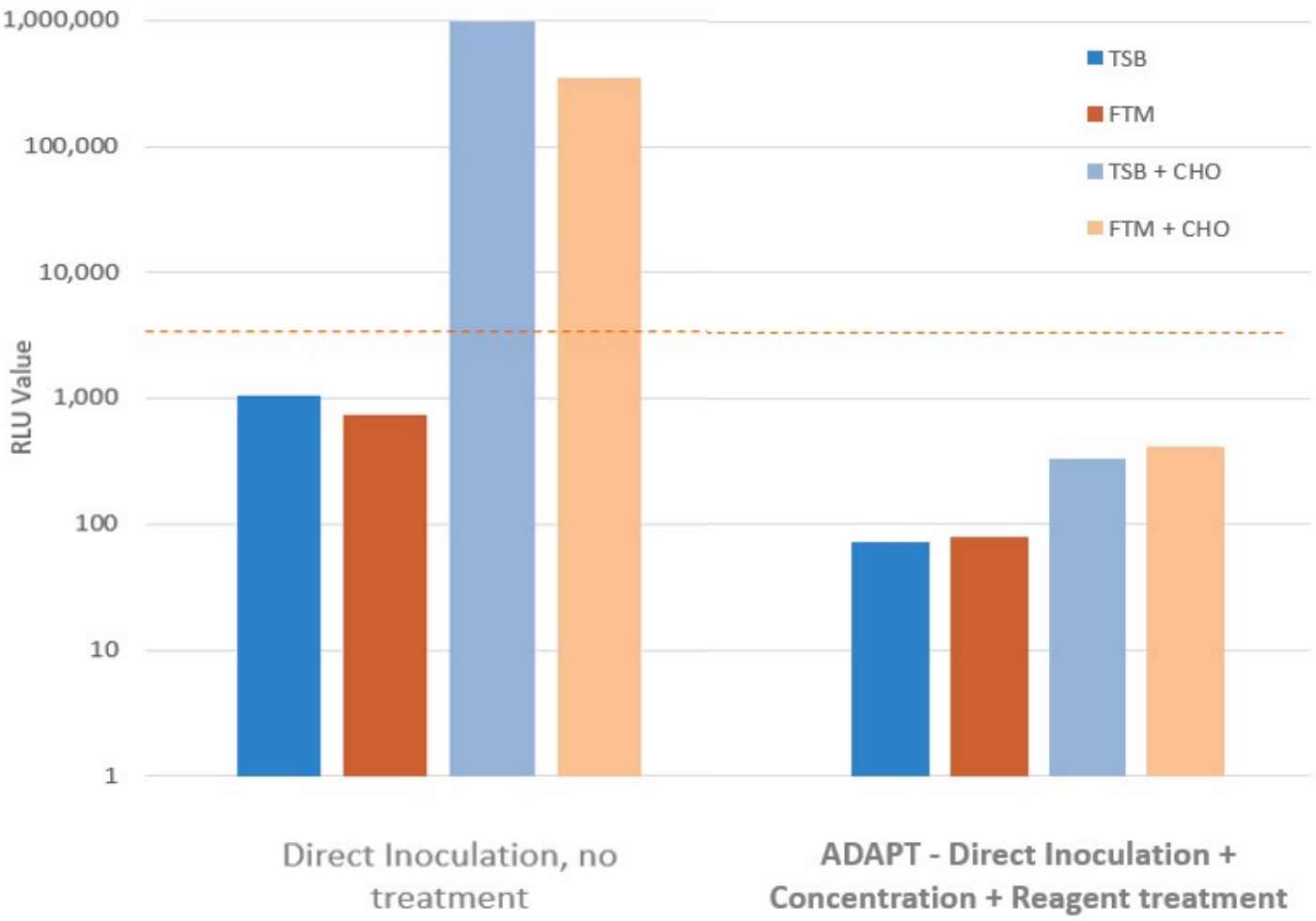
REDUCTION OF ATP BACKGROUND

Background of 10 mL Cell Sample (CHO, $1x10^6$ / mL) + 100 mL TSB/FTM



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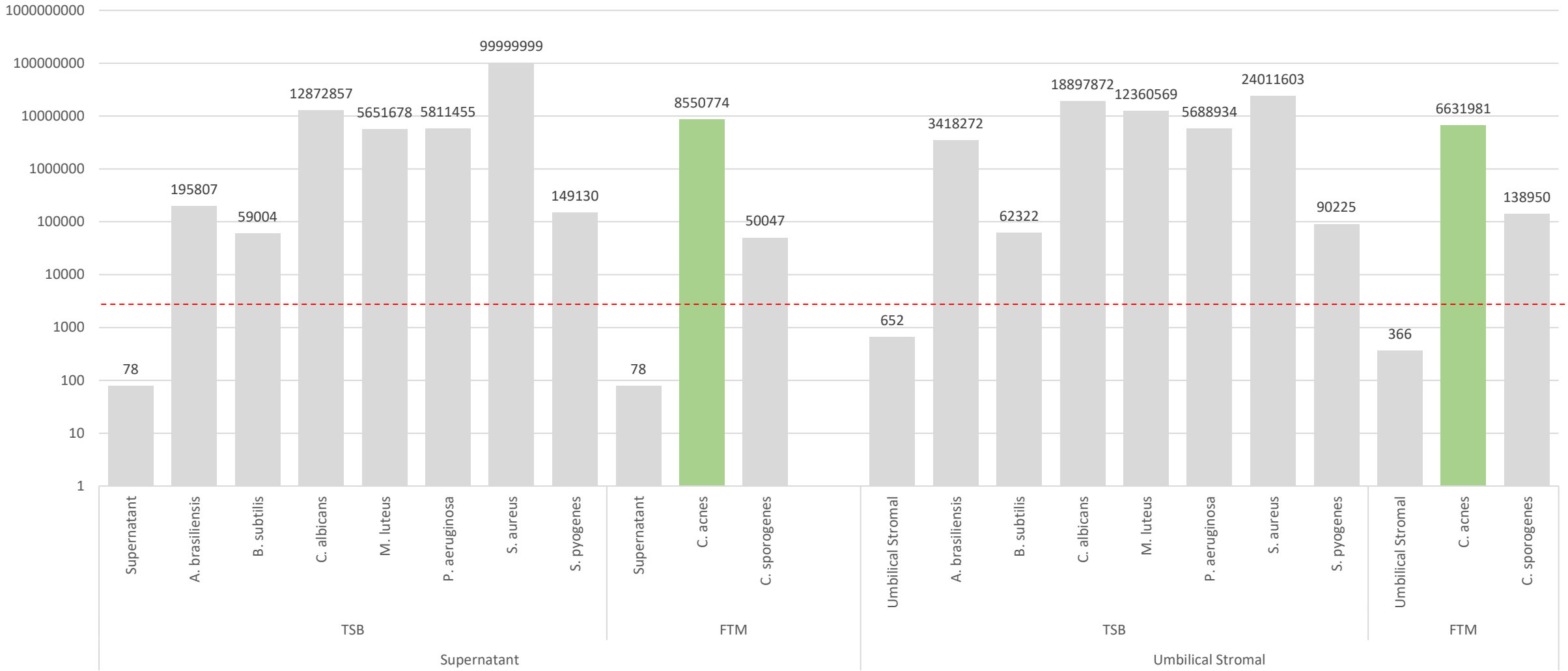
STEM CELLS METHOD SUITABILITY (PH. EUR. 2.6.27)

1 mL Human Umbilical Stromal Cells ($5x10^6$ / mL) and Supernatant + 100 mL TSB/FTM, **7 Days Incubation**



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CELSIS DATA AND VALIDATION SUPPORT

CELL LINE COMPATIBILITY

Celsis Adapt™ Cell

The testing system has undergone rigorous compatibility testing with commonly used cell lines in biopharma processing and cell-based production. This growing list of cell lines include, but are not limited to, the following cell types:

- A9 (Mouse)
- Adipose Stromal Cells (Human)
- ATCC® VR-844™(Murine Sarcoma Virus)
- BALB 3T3(Mouse embryo fibroblast)
- CEF (Chicken embryo fibroblast)
- CEL (Chicken embryo liver cells)
- CHO-K1 (Cricetulus griseus, Chinese Hamster ovary)
- CHO-DG44
- CHO-BHK21(Baby hamster kidney cell)
- HEK-293 (Human embryonic kidney)
- HeLa (Human)
- MDBK (Madin-Darby bovine kidney)
- Mesenchymal stromal cells
- Mrc-5 (Medical Research Council cell strain 5)
- PG4 (S+L- Cat)
- S+L- Mink
- TK6 (Homo sapiens spleen lymphoblast)
- Umbilical Stromal Cells (Human)
- Vero (African green monkey kidney epithelial)
- XC-Rat

UNDERSTANDING THE RELEASE TESTING OPTIONS

Multiple Opportunities to Release Product Faster

3day
RELEASE TEST
Using USP <1071> and Ph. Eur. 2.6.27 approach for ATMPs and short shelf-life products. Utilizes

4day
STERILITY TEST
In accordance with USP <71>, Ph. Eur. 2.6.1, but utilizes a 3rd incubation parameter of TSB at

7day
STERILITY TEST
In accordance with USP <71>, Ph. Eur. 2.6.1, and utilizes compendial incubation parameters.

ALTERNATIVE METHOD VALIDATION REQUIREMENTS

Requirements		Required By			Definition	Charles River Support
POC	Proof of Concept	✓		✓	Feasibility or principle (i.e., assessing whether the method and accompanying system is suitable for its intended purposes and that it is compatible with the intended product or sample matrix.)	Celsis® Sample Effects and Spiking Studies performed in Applications Lab
Instrument Qualification	Installation Qualification	✓	✓	✓	Analytical equipment was installed correctly.	Celsis Advance II™ Installation Qualification
	Operational Qualification	✓	✓	✓	Analytical equipment meets the manufacturer's specification for correct operation.	Celsis Advance II™ Operational Qualification
	Performance Qualification	✓	✓	✓	Instrument meets the URS (User Requirements) for performance.	Celsis Advance II™ Performance Verification *Additionally, user must complete internal performance qualification requirements as deemed appropriate by the user*
Validation of Alternate Technologies	Specificity	✓	✓	✓	Method's ability to detect a range of challenge microorganisms, which demonstrate that the method is fit for its intended use.	Celsis® Sterility Equivalency (Membrane Filtration) – Report (VAL4000EQ)
	Limit of Detection	✓	✓	✓	The lowest number of microorganisms in a defined volume of sample that can be detected, but not necessarily quantified, under the stated experimental conditions.	
	Equivalence/ Comparative Testing/ Accuracy	✓	✓	✓	When the test results from two procedures are sufficiently close for the intended use of the procedures. Demonstration of equivalence requires a prespecified measure of how similar the test results need to be. (e.g. statistical test, e.g. non-inferiority).	
	Robustness	✓	✓	✓	A capacity of the method to remain unaffected by small but deliberate variations in method parameters, e.g., reagent volume, incubation time, or ambient temperature, providing an indication of its reliability during normal usage.	The Celsis AMPiScreen® Rapid Detection Assay Verification of Robustness – Report (TRCELSIS-06.0)
	Ruggedness		✓	✓	The degree of precision of test results obtained by the analysis of the same samples under a variety of typical test conditions such as different analysts (for example, three), instruments, and reagent lots.	The Celsis AMPiScreen® Rapid Detection Assay Verification of Ruggedness – Report (TRCELSIS-05.0)
	Repeatability		✓		The degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings of the same suspension of microorganisms and uses different suspensions across the range of the test.	Dependent upon application; support provided as needed.
Method Suitability	Suitability	✓	✓	✓	Demonstrates that the new method is compatible with specific product or sample matrices that will be routinely assayed, each material should be evaluated for the potential to product interfering or abnormal results, such as false positives or false negatives.	Method Suitability Test
	Equivalence/ Comparative Testing	✓	✓	✓	When comparing two test procedures to show equivalent or better performance, statistical evidence is assembled to show equivalence or, in statistical terms, non-inferiority in presence of product.	Equivalence demonstration in presence of product to include relevant environmental isolates

VAL6000MF: *Celsis Complete for Sterility Membrane Filtration* – Comprehensive GMP Service for validation, including protocol support for method transfer.

VAL6100MF: Celsis Advantage for Sterility Membrane Filtration – Full documentation package to include primary validation reports and protocols for demonstrating method suitability

Each customer is responsible for consulting internal quality requirements and Regulatory authority, as appropriate, for validation requirements.

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CONTACT US

Jon Kallay
Senior Technical and Market Development Manager
Jonathan.kallay@crl.com

Address:
251 Ballardvale Street
Wilmington, MA
01887

Email:
askcharlesriver@crl.com

Website:
www.criver.com

Phone:
877.CRIVER.1

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