2024 NIST RMTM Consortium Workshop Agenda

Thursday, April 11, 2024 – Friday, April 12, 2024
Virtual Workshop

WORKSHOP OVERVIEW

The NIST-led Rapid Microbial Testing Methods (RMTM) Consortium launched in 2020 to develop standards and measurement-based solutions to advance the use of RMTMs in advanced therapy products. NIST is hosting the 4th annual workshop on RMTMs to update the community on RMTM Consortium efforts and to work on Consortium deliverables. Over the course of two days, independent working sessions (1 h to 2 h in length) will be hosted, with Day 1 open to the public and Day 2 for Consortium members only. This virtual workshop is free of charge. All interested parties are invited to Day 1, including advanced therapy producers, RMTM assay/instrument developers, and cell reference material producers. New members are being accepted into the Consortium.

AGENDA

Day 1: Thursday, April 11, 2024 (Sessions OPEN to all registrants, times listed in ET)

Time (ET, Duration)	Session
9:45 am - 10:00 am	**Welcome Remarks and Workshop Overview**
10:00 am - 12:00 pm	**Next Generation Sequencing (NGS)-Based Sterility Testing** **Abstract:** ● Discuss the development of NGS-based analysis tools for microbial sterility testing in the biomanufacturing environment. Includes the development of custom reference genome/gene databases, bioinformatic pipelines, and standardized reporting formats.
12:00 pm - 1:00 pm	**Lunch**
1:00 pm - 2:00 pm	**NIST RMTM Consortium Update** **Abstract:** ● Overview of the NIST RMTM Consortium and updates on Working Group activities.
2:00 pm - 2:15 pm	**Break**
2:15 pm - 3:30 pm	**Developments in RMTM Technology** This session will focus on new technologies and adoption of non-compendial methods for Microbial Testing ● **Development of a Next Generation Sequencing Workflow for Rapid Microbial Testing** Neeraj Salathia (Resilience) ● **CalScreener+ for rapid phenotypic sterility test method for direct inoculation of ATMPs** Wilhelm Paulander (Symcel)

2024 NIST RMTM Consortium Workshop Agenda

Thursday, April 11, 2024 – Friday, April 12, 2024
Virtual Workshop

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	• **Commercial Cell Therapy Experience implementing Rapid Microbial Testing Methods** John Duguid (Vericel Corporation)
3:30 pm - 3:45 pm	**Break**
3:45 pm - 4:50 pm	**Roadmap for Microbial Cell Reference Material Characterization** **Abstract:** • Overview and discussion of a draft roadmap to optimize methods for total cell count and total genome count on microbial cell reference materials. Gather input to refine technical considerations in the roadmap.
4:50 pm - 5:00 pm	**Day 1 Wrap-up**
5:00 pm	**Adjourn**

Day 2: Friday April 12, 2024 (Sessions are for Consortium members only, times listed in ET)

Time (ET, Duration)	Session
9:00 am - 9:05 am	**Welcome and Introduction**
9:05 am - 10:30 am	**RMTM Interlaboratory Study Discussion (closed)** **Abstract:** • Interlaboratory Studies Working Group will present the plan (including draft experimental protocol and timeline) for the second RMTM interlaboratory study followed by open discussion and revisions.
10:30 am - 10:45 am	**Break**
10:45 am - 12:15 pm	**New Study: Quantification of Total Cell Count for Compendial Organisms (closed)** **Abstract:** • Discussion of the technical plan for quantifying total cell count in USP <71> compendial microorganisms, including identification of appropriate strains, potential inclusion of commercial materials, and selection of measurement methods. This study will evaluate the method optimization roadmap for cell count in terms of fitness-for-purpose and robustness across microbial strains.
12:15 pm - 1:15 pm	**Lunch**
1:15 pm - 3:15 pm	**Validation Strategies Workflow (closed)** **Abstract:**

2024 NIST RMTM Consortium Workshop Agenda

Thursday, April 11, 2024 – Friday, April 12, 2024
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	● Discussions on how to develop validation strategies for adopting new RMTMs in the current Good Manufacturing Practice (cGMP) biomanufacturing environment. Includes topics related to: what to sample, reference materials, experimental design, statistical analysis, and assessing analytical performance.
3:15 pm - 4:00 pm	**Workshop Summary, Open Dialogue, and Next Steps**
4:00 pm	**Adjourn**

SPEAKERS (in order of appearance)

Scott Jackson, Ph. D. (NIST)

- Dr. Scott Jackson joined The National Institute of Standards and Technology (NIST) in May of 2014. At NIST, Scott is the founder and leader of the Complex Microbial Systems Group. In this current role, Scott is leading international efforts to improve microbiome and metagenomic measurements by organizing inter-lab studies, developing reference materials, and reference methods.

  Prior to joining NIST in 2014, Scott spent 11 years as a principal investigator at FDA where he developed advanced genomic tools for characterizing the global genomic diversity of enteric pathogens, with applications in food safety, bioforensics and public health. Scott completed his PhD research in biochemistry and biophysics at The University of Maryland and Johns Hopkins University, respectfully, where he focused on the evolution of mobile genetic elements. Scott performed his undergraduate studies in Chemistry and Geology at the University of South Carolina

Nancy Lin, Ph. D. (NIST)

- Dr. Nancy Lin is the Leader of the Biomaterials Group in the Biosystems and Biomaterials Division at the National Institute of Standards and Technology. Her research focuses on developing measurements and standards to enable detection, characterization, and quantification of microbes and microbial communities, with an emphasis on microbial cell reference materials, biofilm-material interactions, antimicrobial efficacy, microbiome, and biosurveillance. Nancy holds a BS in Mechanical Engineering from Valparaiso University and a PhD in Biomedical Engineering from Case Western Reserve University.

Wilhelm Paulander, Ph. D. (Symcel)

- Dr Wilhelm Paulander is a microbiologist with a background in academic research from Copenhagen University, Karolinska Institute and UC Davis within the field of antibiotic resistance and as CSO at 1928Diagnostics responsible for working on the development of next-generation sequencing techniques for diagnostics applications. Wilhelm joined Symcel in 2018 as Chief Clinical Development Officer responsible for the adaptation of the calScreener technique for applications in diagnostics of bone and joint infections and rapid detection of microorganisms in sterility testing, focusing on ATMPs.

Neeraj Salathia, Ph. D. (Resilience)

2024 NIST RMTM Consortium Workshop Agenda

Thursday, April 11, 2024 – Friday, April 12, 2024
Virtual Workshop

- Neeraj Salathia is the Director of the Advanced Genomics team at Resilience, based in San Deigo. His team is deeply involved in developing novel genomics solutions towards rapid microbial testing. Neeraj has deep experience in developing single cell and bulk Next Generation Sequencing (NGS) assays in his current, as well as previous roles at Celgene, BMS, Molecular Stethoscope and Illumina.

John Duguid (Vericel Corporation)

- John Duguid is Executive Director, Research & Development at Vericel, where he is the CMC technical lead for commercial-stage autologous cell therapy products. Previously a Principal Scientist at Genzyme, Mr. Duguid was responsible for developing and implementing rapid microbiological methods and had also managed QC operations. Prior to Genzyme, he worked as an analytical chemist at Abbott Laboratories and Arthur D. Little. Mr. Duguid received his BS in Chemistry from the University of Michigan.

Kirsten Parratt, Ph. D. (NIST)

- Dr Parratt joined the NIST Biomaterials Group in 2018. She works on projects related to microbial characterization and enumeration, and research data management. Her doctoral research in Prof Krish Roy's research group at the Georgia Institute of Technology focused on biomaterials-driven stem cell differentiation paired with imaging flow cytometry.

Stephanie Servetas, Ph. D. (NIST)

- Dr. Stephanie Servetas is a microbiologist in the Complex Microbial Systems Group at NIST. Her research focuses on whole cell and multi-omic measurements of microbial communities, both natural and contrived. While at NIST, she has worked on the development of several reference materials for biosurveillance and microbiome measurements. Stephanie arrived at NIST in 2018 after completing her PhD in Emerging Infectious Diseases at the Uniformed Services University in Bethesda, Maryland.

Monique Hunter, MS (NIST)

- Monique Hunter is a research microbiologist in the Complex Microbial Systems Group at NIST. She joined the group in 2019 and works on projects related to microbial characterization, enumeration and developing molecular methods. She received her Master's in Biology from George Mason University, Virginia.

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DETAILED AGENDAS

Day 1

Opening Remarks: Scott Jackson and Nancy Lin - Overview of the 2024 NIST RMTM Consortium Workshop Agenda and Goals

SESSION 1: Next Generation Sequencing (NGS)-based Sterility Testing

SESSION MODERATOR(S): Scott Jackson

GOAL STATEMENT: Strategize on development of custom NGS-based tools to support sterility testing in biomanufacturing

SESSION/SPEAKER BREAKDOWN:

Discuss the development of NGS-based analysis tools for microbial sterility testing in the biomanufacturing environment. Includes the development of custom reference genome/gene databases, bioinformatic pipelines, and standardized reporting formats.

PRESENTATION: (30 min)

DISCUSSION: (90 min)

SESSION 2: NIST RMTM Consortium Update

SESSION MODERATOR(S): Nancy Lin

GOAL STATEMENT: Provide Update on the NIST RMTM Consortium's Progress and Outputs

SESSION/SPEAKER BREAKDOWN: Nancy Lin (NIST)

PRESENTATION (45 min)

DISCUSSION (15 min)

SESSION 3: Developments in RMTM Technology

SESSION MODERATOR(S): Stephanie Servetas (NIST)

GOAL STATEMENT: Discuss and assess both new and available non-compendial methods for rapid microbial testing from an end-user perspective to identify challenges to adoption and future prospects.

SESSION/SPEAKER BREAKDOWN:

PRESENTATIONS (50 min):

Wilhelm Paulander (SYMCEL)

Abstract: We have developed a novel instrument based on isothermal microcalorimetry, enabling continuous monitoring of metabolic activity from a broad range of contaminating microorganisms in a non-destructive and product-matrix-independent manner. The method

requires a minimal sample volume of 0.05 mL and delivers results within 3 days for detection of contaminants, with a limit of detection (LOD) <5 CFU. Its high resolution (< 1 µW) enables the detection of low-level contaminants even in complex matrices with high (>10e6 cells/mL) eukaryotic cell background. For example, in Jurkat cells at <5 CFU/mL, *S. aureus*, *P. aeruginosa*, *B. subtilis*, *C. sporogenes* and *C. albicans* are all detected in less than 24 hours, *A. brasiliensis* in around 30 hours and *C. acnes* in 72 hours.

Neeraj Salthia (RESILIENCE)

Abstract: Resilience is developing a novel next generation sequencing (NGS) -based approach for rapid microbial QC testing in biomanufacturing. We will highlight our workflow and analytical approaches to expedite and deeply characterize drug product for safety testing. Additionally, regulatory strategy and considerations will be discussed.

John Duguid (VERICEL)

Abstract: Rapid detection of contaminants is essential for cell therapy products with short shelf lives. Final product release tests that require minimal sampling, produce rapid valid results, and are inexpensive to use are critical to allow final product lot release prior to product expiration and surgical implantation. Implementation of the first rapid sterility test for lot release of a biologic occurred in 2004 followed by the first rapid mycoplasma test using real-time PCR in 2013.

DISCUSSION (25 min)

SESSION 4: Roadmap For Microbial Cell Reference Material Characterization

SESSION MODERATOR(S): Nancy Lin (NIST)

Goal statement: Discuss potential technical avenues to obtain total cell count and genome count certified values for existing microbial cell reference materials

SESSION/SPEAKER BREAKDOWN:

Presentation (30 min) Kirsten Parratt (NIST)**:** Overview of a draft roadmap to optimize methods for total cell count and total genome count of microbial cell reference materials

Discussion (35 min)

- Gather input to refine technical considerations in the roadmap
- What level of agreement is needed between methods?
- How could this roadmap be transferred to manufacturers? What portions are infeasible?

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DAY 2 (CONSORTIUM MEMBERS ONLY)

SESSION 1: RMTM Interlaboratory Study Discussion (closed)

SESSION MODERATOR(S): Stephanie Servetas (NIST)

GOAL STATEMENT: Obtain input from the community on the second RMTM interlab study**.**

SESSION/SPEAKER BREAKDOWN: Stephanie Servetas (NIST)

PRESENTATION & DISCUSSION (90 min): Proposal for the 2nd RMTM Consortium Interlaboratory Study

SESSION 2: New Study: Quantification of Total Cell Count for Compendial Organisms

SESSION MODERATOR(S): Nancy Lin, Kirsten Parratt

GOAL STATEMENT: To obtain input from the community on future WG1 technical studies

SESSION/SPEAKER BREAKDOWN:

Presentation (Monique Hunter, NIST) (20 min): Preliminary Results on Multi-Method Quantification of Compendial Organisms

Discussion (70 min):

- Technical plan for quantifying total cell count in USP <71> compendial microorganisms
- Application of roadmap, technical plan design
- Identification of appropriate strains, potential inclusion of commercial materials, and selection of measurement methods

SESSION 3: Validation Strategies Workflow

SESSION MODERATOR(S): Scott Jackson

GOAL STATEMENT: Host a discussion on approaches towards validation of alternative (rapid) methods for microbial sterility testing.

SESSION/SPEAKER BREAKDOWN: Discussions on how to develop validation strategies for adopting new RMTMs in the current good manufacturing practice (CGMP) biomanufacturing environment. Includes topics related to: what to sample, reference materials, experimental design, statistical analysis, and assessing analytical performance.

Presentation (30 min)

Discussion (90 min)