ANTI-BIOFILM TECHNOLOGIES

PATHWAYS TO PRODUCT DEVELOPMENT

Jan. 31—Feb. 1, 2024

Renaissance Arlington Capital View Hotel

Executive Proceedings

CENTER FOR BIOFILM ENGINEERING

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Exhibitor:

BioSurface Technologies
Providing innovative products for biofilm investigations
Bozeman, MT
Attending: Bryan Warwood, CEO
https://biofilms.biz/

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Keynote Presentation:

Antimicrobial-containing wound care devices: Navigating the regulatory landscape

Brandon Kitchel
Microbiologist/Expert Reviewer, Office of Surgical and Infection Control Devices, US FDA

Purpose/Methods/Next Steps:
Our keynote presentation will provide an invaluable regulatory perspective for evaluating antimicrobial-containing wound care devices, including outlining product jurisdiction and device classification considerations that dictate the regulatory pathways needed for these products to reach the market. Additionally, this talk will break down the understood performance claims and supporting testing needed to demonstrate the roles of the antimicrobial components in wound care devices currently on the market. While there are understood gaps in wound care needs (e.g., chronic and non-healing wounds), this presentation will help detail some of the challenges faced with supporting biofilm-related claims in this device space, and highlight the various mechanisms the FDA has worked to support device innovation to help improve our overall wound care outcomes.

SESSION 1: Wounds & NTM Lung Infections

Microbiome of venous leg ulcers

Garth James
PI, Medical Biofilms Laboratory, Center for Biofilm Engineering
Associate Research Professor, Chemical & Biological Engineering, Montana State University

Purpose of this Research:
Bacteria may influence healing, inflammation, and symptoms of venous leg ulcers (VLU). This research characterized the bacteria present in tissue specimens from subjects during treatment of chronic VLU.

Methods and Results:
DNA was extracted from 345 wound debridement specimens from 107 subjects at up to 5 timepoints over an 8-week treatment period, amplicons from the bacterial 16S rRNA genes were sequenced and analyzed to identify the genera present. Of 90 different genera with a relative abundance greater than 1%, *Corynebacterium*, *Pseudomonas* and *Staphylococcus* were predominant. Other abundant genera were *Alcaligenes*, *Finegoldia*, *Klebsiella*, *Proteus*, *Ralstonia*, *Serratia*, and *Streptococcus*.

Next Steps:
The influence of the bacterial genera present on wound healing trajectory, inflammation, and symptoms will be evaluated.

Industrial Relevance:
It was estimated in 2019 that 500,000 to 600,000 people in the US had VLU, resulting in serious impacts on health and quality of life as well as $1 billion in healthcare costs. The global market for VLU treatment products is expected to reach $4.8 billion by 2026.

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Clinical studies interrogating the prevention and treatment of surgical site infections and chronic wounds

Sybil D'Costa Ph.D.
Sr. Manager, Clinical Operations, Next Science, LLC.

Purpose of this Research:
The Next Science XBIO® technology is designed on material science principles to solve the challenge of biofilm-related infections. The collective goal of the research is to evaluate the clinical safety and efficacy of the suite of wound care and surgical products developed on the XBIO platform.

Methods and Results:
The presentation elucidates findings using 2 FDA cleared products; BlastX® Antimicrobial Wound Gel in the management of chronic wounds, and XPERIENCE® Advanced Surgical Irrigation as an intraoperative cleanser. Post market clinical studies were completed to evaluate clinically relevant endpoints like wound area reduction and rates of surgical site infections. The products exhibited significant improvements in the endpoints evaluated in the clinical trials.

Next Steps:
The next steps of the research include filling in the current knowledge gaps to elucidate mechanisms of activity in clinical settings, by utilizing innovative genomic, proteomic, and cellular assays.

Industrial Relevance:
These studies are critically relevant in the healthcare industry where biofilms are estimated to be responsible for 80% of chronic infections, 60% of all human bacterial infections and in hospital settings where biofilms are implicated in more than 65% of nosocomial infections.

Laboratory testing of antimicrobial activity and innate immune system compatibility

Philip Stewart
Regents Professor of Chemical and Biological Engineering

Purpose of this Research:
The goal of this research was to provide an in vitro assessment of both the antimicrobial efficacy and the immune system compatibility of three surgical lavage solutions. While antimicrobial and antibiofilm effects are routinely measured, the impact of antiseptics on innate immune cells such as neutrophils is rarely evaluated.

Methods and Results:
Antimicrobial activity was evaluated by measuring the minimum inhibitory concentration and by video microscopy of the enlargement or shrinkage of bacterial aggregates exposed to the test solutions. Neutrophil compatibility was evaluated by quantifying the motility and viability of human neutrophils exposed to the test solutions. The solutions all exhibited antimicrobial activity, but showed variation in their degree of compatibility with neutrophil function.

Next Steps:
Because preventing infections involves contributions from both antimicrobial chemotherapy and the host innate immune system, it is suggested that in the development of antibiofilm technologies, evaluation of innate immune system compatibility with antimicrobial agents or antibiofilm surfaces could be valuable.

Industrial Relevance:
Development of new products that prevent infections on or around medical devices could be aided by incorporating testing of the compatibility of antimicrobial technology with the healthy functioning of innate immune cells.

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Flying under the radar: Mycobacterium abscesses - a stealthy pathogen?

Luanne Hall-Stoodley
Associate Professor, Microbial Infection and Immunity, The Ohio State University College of Medicine

Purpose of this Research:
My research focuses on bacterial pathogens that infect the human airways, including the understudied nontuberculous mycobacterium, *Mycobacterium abscessus*, which causes life-threatening chronic infections in people with muco-obstructive lung diseases. I want to understand how these pathogens evade host defenses and antibiotic therapies and contribute to persistent lung infections.

Methods and Results:
Many human chronic respiratory infections are not well-recapitulated in mouse models. To address this, I have developed human primary cell models to interrogate recurrent infections. Using sputum and primary human air-liquid interface (ALI) differentiated airway epithelial cells, we have shown that aggregates form under some but not all circumstances and targeting aggregates can lead to better efficacy with antibiotics.

Next Steps:
I am interested in understanding the determinants and drivers of persistent bacterial infections and particularly how these may be used in adjunctive or combination therapies to eradicate infections.

Industrial Relevance:
I use translationally relevant cell models to interrogate therapeutically challenging bacterial pathogens.

Aerosolized bacteria: From world-wide infections to addressing regulatory science needs

Jon Weeks
Acting Assistant Director, Sterility & Infection Control Program, CDRH, US FDA

Purpose of this Research:
The goal of the research was to develop a method to assess the aerosolization potential of nontuberculous Mycobacteria (NTM) from solutions and compare the differences between two different Mycobacterium species. We also aimed to develop a positive control that could be used for aerosol testing from heater cooler devices.

Methods and Results:
Our results increasing flow rate/vigorousness of bubbling also increased the amount of NTM that were aerosolized. We demonstrated that both inoculum concentration and flow rate/vigorousness of bubbling increased the number of both species. Finally, our results demonstrated that *M. chimaera* was more prone to aerosolization, especially at lower inoculum concentrations.

Next Steps:
For our purposes, this particular research has concluded. If someone was to continue this research, the next step would be to see if there was another NTM species that grows faster, is in a lower risk group or lower risk of respiratory infection, that shows similar production of aerosols at low inoculum concentration and flow rates that could be used as a surrogate for aerosolization testing.

Industrial Relevance:
The current technical protocols may assist medical device manufacturers or third-party testing facilities with testing aerosol emission from HCDs.

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SESSION 2: Self-Regulating Industries

What's the deal with the ADA Seal?

Prerna Gopal
Senior Manager, Seal and Standards, American Dental Association

Purpose of this Research:
An unbiased program to measure the safety and efficacy of over-the-counter dental care products.

Methods and Results:
Products are tested and evaluated via laboratory testing and independent scientific review for specific aspects of the product, such as its ingredients, formulation, and performance.

Next Steps:
New innovative products submitted to the ADA pave the way for new standards and clinically-relevant *in vitro* testing that helps to maintain the patient's safety.

Industrial Relevance:
In collaboration with industry, the ADA Seal program helps bridge the gap between research and clinical application of the products, thereby enhancing the oral care standards.

Viscoelasticity as a therapeutic target to remove dental biofilms

Erin Gloag
Assistant Professor, Department of Biomedical Sciences and Pathobiology, Virginia Polytechnic University

Purpose of this Research:
Understand how dentifrice treatment impacts mechanical properties of dental biofilms.

Methods and Results:
Dental-plaque biofilms were treated with dentifrice solutions and mechanical properties analyzed by either uniaxial indentation or rotating-disc rheology. We found that arginine can disrupt biofilm stability and enhance biofilm removal by shear forces.

Next Steps:
Look further into the changes in EPS chemistry upon dentifrice treatment.

Industrial Relevance:
Assist industry partners in developing new products and provide a greater understanding of the mechanism of action.

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How cross sector collaboration helped define benchmarks used for OTC antimicrobial mouth rinses

Michael Lynch
Director, Fellow, Global Scientific Engagement, Oral Health, Kenvue

Purpose of this Research:
To provide a historical perspective on how constructive interactions between multiple organizations helped shape the ADA Guidelines for the Seal of Acceptance in the OTC antimicrobial mouth rinse category.

Methods and Results:
In 1972, the US FDA established the OTC drug monograph process. This talk will focus on some of the history of the anti-gingivitis/antiplaque drug products category and how industry has worked with groups - including the ADA, CHPA, and academia - over the past several decades, to establish criteria for the determination of safety and efficacy for this category.

Next Steps:
In 1985, the ADA established criteria for the Seal of Acceptance for this OTC rinse category. This led to Listerine being awarded the Seal in 1987.

Industrial Relevance:
The ADA Seal is well-recognized and valued by consumers and dental professionals when looking for safe and effective oral care products.

Pathways for personal care product registration: Cosmetic vs. over-the-counter drug vs. new drug approval

James W. Arbogast, Ph.D.
Principal Consultant, JW Arbogast Advanced Science Consulting LLC

Purpose of this Research:
The purpose of this presentation is to compare and contrast the differences between a Cosmetic vs. OTC (over-the-counter) vs. NDA (new drug approval) new product launch. This will be framed to highlight the impact on product development efforts and the US personal care market overall.

Methods and Results:
Information will be gathered and summarized with an emphasis on US FDA guidance/rules and industry implications. Examples will be shown to demonstrate how the personal care product registration framework impacts new products and innovation.

Next Steps:
If any conference attendees want to go deeper into this topic, I would be happy to collaborate.

Industrial Relevance:
This presentation is educational in nature and hopefully will help industry personnel learn plus improve their approach to new personal care product development in the future.

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SESSION 3: Hard Surface Disinfection

Quantitative efficacy assessment of antimicrobials against bacteria, spores, viruses, and fungi

Rebecca Pines
Chief, Microbiology Laboratory Branch, US EPA

Purpose of this Research:
To demonstrate use of the Quantitative Method to assess multiple classes of microbes (e.g., bacteria, viruses, spores, fungi) against a variety of antimicrobial products.

Methods and Results:
The Quantitative Method is currently going through ASTM for testing against *S. aureus* and *P. aeruginosa* and has been the subject of several multi-laboratory collaborative assessments. The method has also been successfully used internally to assess efficacy of antimicrobials against a tuberculosis surrogate, *Bacillus* spores, viruses, and fungi.

Next Steps:
Continue to pursue standardization of the Quantitative Method through ASTM (e.g., *Salmonella enterica* multi-laboratory study).

Industrial Relevance:
The Quantitative Method (QM) is currently used for registration of public health antimicrobials against *Candida auris*, spores of *Clostridioides difficile*, and for registration of disinfectants for use on soft surface textiles. The QM is versatile and could be proposed as an alternative means for registering antimicrobials.

Statistical considerations of presence/absence assays in microbiology

Al Parker
Biostatistician, Center for Biofilm Engineering
Associate Research Professor, Mathematical Sciences, Montana State University

Purpose of this Research:
Give an overview of statistical techniques to overcome common roadblocks when analyzing data from presence absence assays.

Methods and Results:
Common statistical methods give overly optimistic results when the resulting data are mostly positives or negatives - in this case use logistic regression. These same methods downright fail when all results are positive or negative - in this case go Bayesian! Aggregate presence/absence results to estimate the number of bugs using the Most Probable Number (MPN) technique. MPN results are comparable to CFU results but with larger variability.

Next Steps:
The statistical methods can be used for determining the limit of detection of the presence/absence assay and for determining how many coupons and tests are needed for validation studies of products, assays, and monitoring systems.

Industrial Relevance:
Applications: Quality control of sterile products; validating presence/absence monitoring systems; presence/absence data generated by antimicrobials can be used to generate a log reduction; in 510k FDA submissions, equivalency of presence/absence results can be assessed using mantra “<0 .5CFU doesn’t matter”.

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The need, or not, for a standardized test method for biofilm kill claims in food production

Bruce Urtz
Microbiology Manager, Sterilex

Purpose of this Research:
To identify a reproducible and challenging test method that can be used to obtain US EPA approved biofilm kill claims for disinfectants used in food processing environments.

Methods and Results:
An EPA accepted protocol involving *Listeria* was evaluated and found to lack reproducibility and generated a low-density biofilm that was easy to kill. Modifications to this method were made that improved repeatability but not biocide resistance. An alternate biofilm method incorporating with Listeria was evaluated which generated significantly higher densities of *Listeria* and was more challenging to kill.

Next Steps:
Short term, identify an external lab capable of running the current EPA accepted protocol. Long term, advocate for a more robust and properly validated method.

Industrial Relevance:
Companies wanting to make biofilm kill claims for disinfectants used in food processing would benefit from a clearer understanding of regulatory expectations and the adoption of properly vetted test methods.

Polymeric n-Halamines for antimicrobial surfaces

Marc Hein
Chief Technology Officer, AvantGuard, Inc.

Purpose of this Research:
We will describe the work being done at AvantGuard to advance the development of n-halamine based polymers for temporary and permanent surface coatings that provide high level antimicrobial performance.

Methods and Results:
AvantGuard synthesizes specialty polymers that impart high level antimicrobial performance when they are treated with chlorine-based cleaning agents. We have demonstrated these polymers can be coated on surfaces to prevent pathogen growth and we have shown that solutions of our polymers can perform in a range and disinfection and antiseptic applications.

Next Steps:
Our next steps are to advance our technology into commercial applications.

Industrial Relevance:
Our coatings are viable solutions in food manufacturing, hospital environments, medical devices, and topical antiseptic solutions.

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New ASTM Quantitative Towelette Method

Ryan Karcher
Biologist, Microbiology Laboratory Branch, US EPA

Lisa Smith
Team Lead, Microbiology Laboratory Branch, US EPA

Purpose of this Research:
EPA may propose an alternative quantitative test method in addition to the currently accepted qualitative methods to obtain efficacy label claims for disinfectant towelettes.

Methods and Results:
Method quantitatively determines the effectiveness of various sizes of antimicrobial towelettes in treating hard, non-porous surfaces against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. This test method does not differentiate between chemical inactivation of the test microbe and mechanical removal of inoculum from a surface; rather, product efficacy is considered a combination of both attributes of a towelette-based formulation.

Next Steps:
Continuation of the interlaboratory studies with a focus on highly-efficacious products. The EPA will propose a guidance document for the newly approved QTM and expanding to other microorganisms.

Industrial Relevance:
A new method for stakeholders to gain label claims against *S. aureus* and *P. aeruginosa* for towelettes.

Center for Biofilm Engineering
a National Science Foundation Engineering Research Center

MONTANA STATE UNIVERSITY

CBE ENGINEERING

Jan. 31 - Feb. 1, 2024

ANTI-BIOFILM TECHNOLOGIES:

Pathways to Product Development

Renaissance Arlington Capital View Hotel, Arlington, VA

2/6/2024 3:15 PM

Final AGENDA

Wednesday January 31

7:30–8:00
Continental Breakfast
Studio B Prefunction Area

Meeting: Studio B

8:00–8:10
Introductory Remarks
Matthew Fields
Director, CBE; Professor, Microbiology & Cell Biology, MSU
Darla Goeres, Industrial Coordinator, Regulatory Research Professor, CBE

Keynote Presentation

8:10–8:55
Antimicrobial-containing wound care devices: Navigating the regulatory landscape
Brandon Kitchel, Microbiologist/Expert Reviewer, Office of Surgical and Infection Control Devices, US FDA

SESSION 1: Wounds & NTM Lung Infections

8:55-9:00
Session Introduction
Kelly Kirker, Assistant Research Professor, Chemical & Biological Engineering, MSU, CBE

9:00–9:30
Microbiome of venous leg ulcers
Garth James, PI, Medical Biofilms Laboratory, CBE; Assoc. Research Professor, Chemical & Biological Engineering, MSU

9:30–10:00
Clinical studies interrogating the prevention and treatment of surgical site infections and chronic wounds
Sybil D'Costa, Senior Manager, Clinical Operations, Next Science

10:00–10:30
Laboratory testing of antimicrobial activity and innate immune system compatibility
Phil Stewart, Regents Professor, Chemical & Biological Engineering, MSU, CBE

10:30–11:00 Break

11:00–11:30
Flying under the radar: Mycobacterium abscesses—a stealthy pathogen?
Luanne Hall Stoodley, Associate Professor, Microbial Infection & Immunity, College of Medicine, The Ohio State University

11:30–12:00
Aerosolized bacteria: From world-wide infections to addressing regulatory science needs
Jon Weeks, Acting Assistant Director, Sterility & Infection Control Program, CDRH, US FDA

12:00–12:15
Session Summary
Kelly Kirker

12:15–1:30 Lunch Studio D

SESSION 2: Self-Regulating Industries

1:30-1:35
Session Introduction
Darla Goeres

1:35–2:05
What's the deal with the ADA Seal?
Prerna Gopal, Senior Manager, Seal and Standards, American Dental Association

2:05–2:35
Viscoelasticity as a therapeutic target to remove dental biofilms
Erin Gloag, Assistant Professor, Microbiology, Virginia Polytechnic Univ.

2:35–3:05
How cross sector collaboration helped define benchmarks used for OTC antimicrobial mouth rinses
Michael Lynch, Director, Fellow, Global Scientific Engagement, Oral Health, Kenvue

3:05–3:35 Break

3:35–4:05
Pathways for personal care product registration: Cosmetic vs. over-the-counter drug vs. new drug approval
Jim Arbogast, President, JW Arbogast Advanced Science Consulting LLC

4:05–4:35
Session Summary
Darla Goeres

4:35–6:00 Networking Reception Studio D

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Thursday
February 1

8:00–8:30
Continental Breakfast
Studio B Prefunction Area

Meeting: Studio B

SESSION 3: Hard Surface Disinfection

8:30–8:35
Introductory Remarks
Darla Goeres

8:35–8:40
Session Introduction
Chris Jones, PI, Standardized Biofilm Methods Lab, CBE

8:40–9:10
Quantitative efficacy assessment of antimicrobials against bacteria, spores, viruses, and fungi
Rebecca Pines, Branch Chief, Microbiology Laboratory Branch, Office of Pesticide Programs, US EPA

9:10–9:40
Statistical considerations of presence/absence assays in microbiology
Al Parker, Biostatistician, CBE; Associate Research Professor, Mathematical Sciences, MSU

9:40–10:10
The need, or not, for a standardized test method for biofilm kill claims in food production
Bruce Urtz, Microbiology Manager, Sterilex

10:10–10:40 Break

10:40–11:10
Polymeric n-Halamines for antimicrobial surfaces
Marc Hein, Chief Technology Officer, AvantGuard Inc.

11:10–11:40
New ASTM Quantitative Towelette Method
Ryan Karcher, Biologist, Microbiology Laboratory Branch, Office of Pesticide Programs, US EPA
Lisa Smith, Team Leader, Microbiology Laboratory Branch, Office of Pesticide Programs, US EPA

11:40–11:55
Session Summary
Chris Jones

11:55–12:00
Closing Remarks
Darla Goeres

Exhibitor:

BioSurface Technologies
Providing innovative products for biofilm investigations
Bozeman, MT
Bryan Warwood, CEO
https://biofilms.biz/

Save the Date!
2024 Montana Biofilm Meeting
July 10-12
Bozeman, MT