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VG-2021-196

Antimicrobial Surface Coatings to Reduce COVID-19 Spread

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Boston University/NEIDL – John H. Connor, Scott Seitz

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Acknowledgement/Disclaimer

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Outline

- **Overview**
  - Technology
  - Background
  - AM Coating
- **Production of Antimicrobial Coated Materials**
- **Characterization**
- **AM Testing**
- **Conclusions**

Technology Overview

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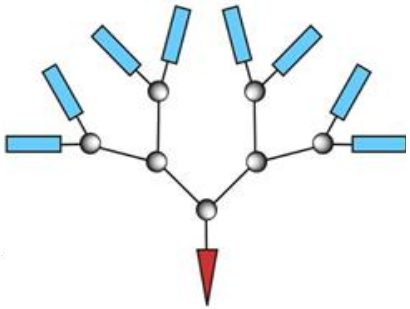
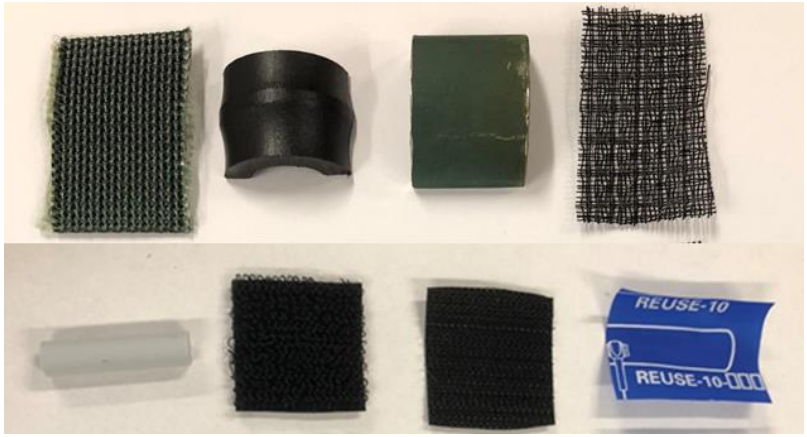
- **Goal**
  - Develop an antimicrobial coating for medical equipment that demonstrate high viral reduction (4 Log reduction, threshold) for VSV & SARS-CoV-2 in a short amount of time (<30min).

A) AM Compound: Molecular design combining high efficacy with strong surface attachment

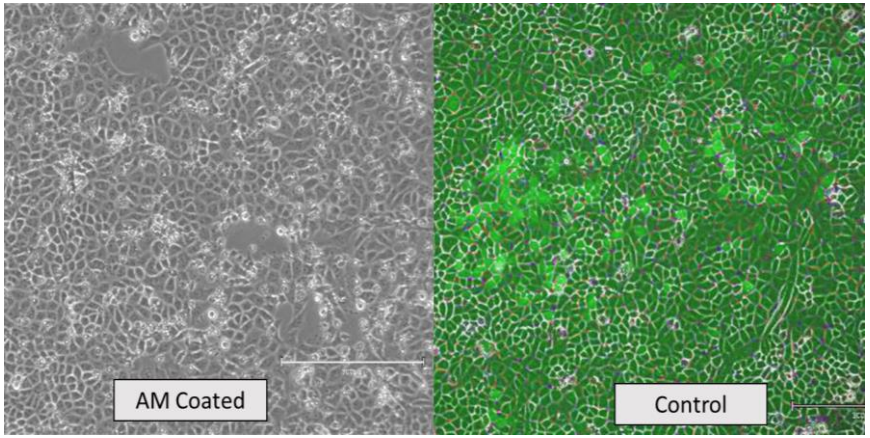


B) Medical Equipment (Evacuation Litter & Blood Pressure Cuff)

C) Coupon Production and Coating

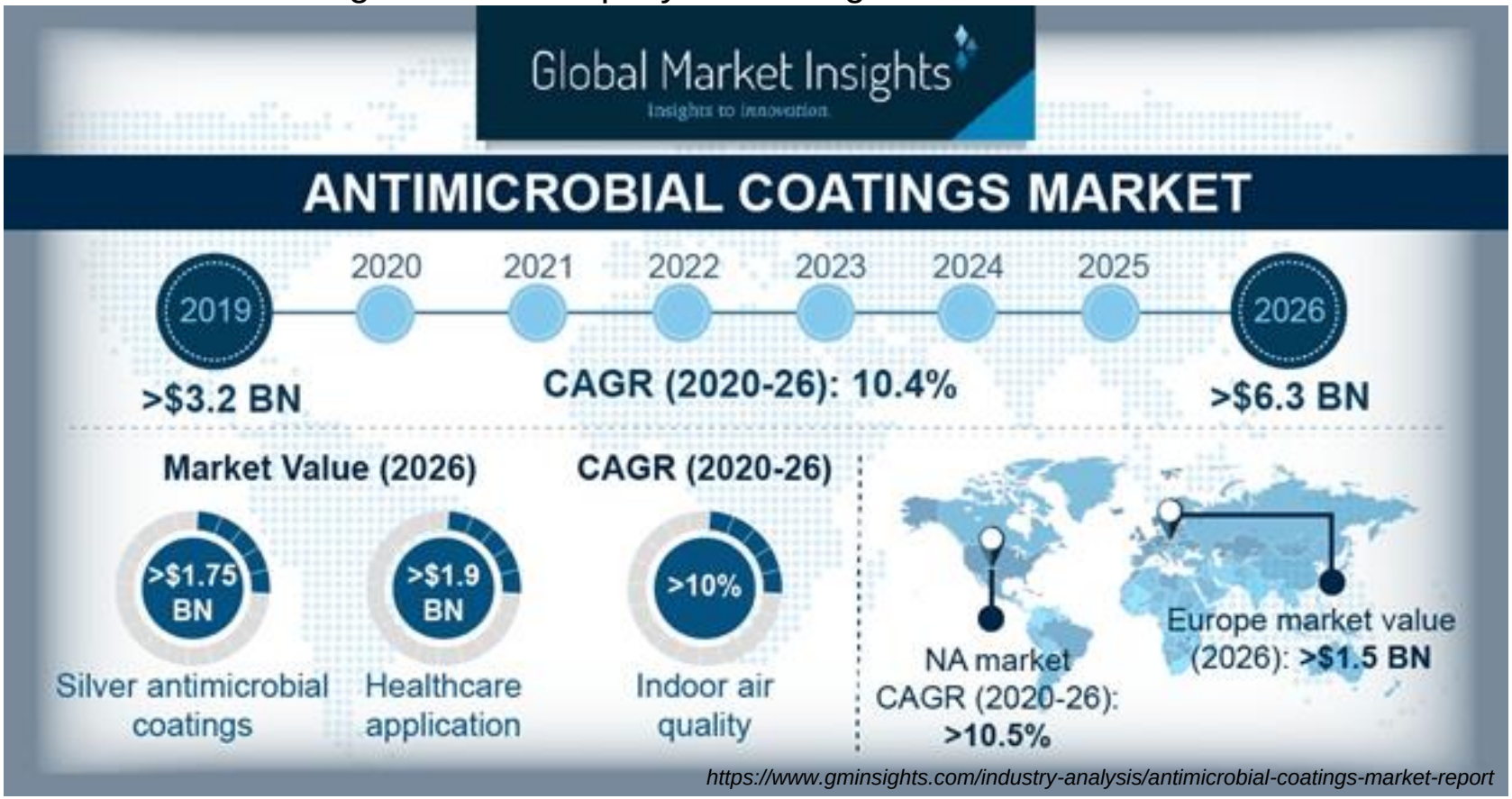


D) Antimicrobial Evaluation



Background

- Strong need for surface decontamination of medical devices and equipment that is long lasting and highly efficacious
- Antimicrobial coatings market is rapidly increasing



Projected high demand for antimicrobial coatings in the healthcare sector (medical devices/equipment)

Antimicrobial Coating Overview

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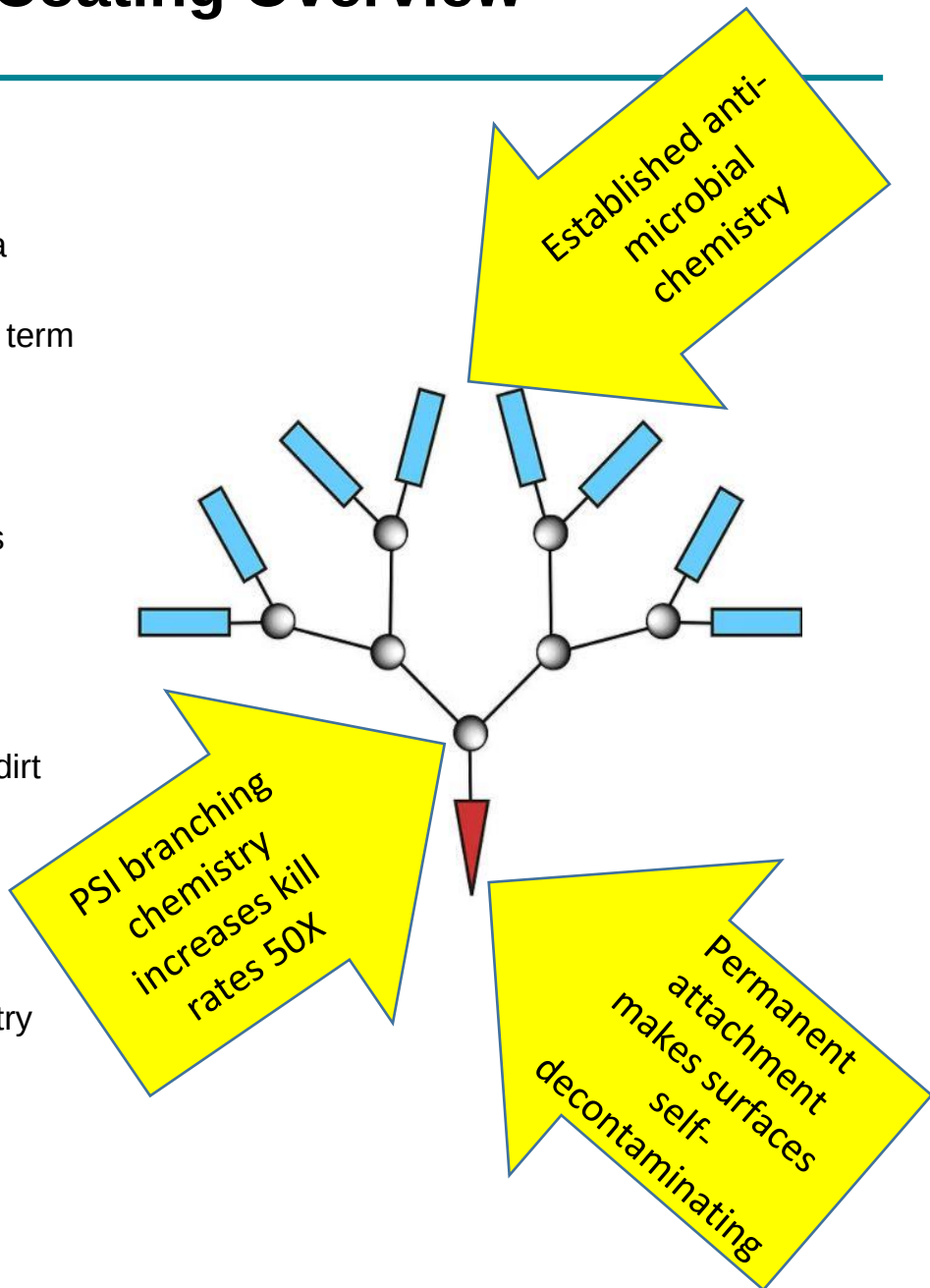
- **Overall need: prevent disease spread from contaminated surfaces**
  - Surface contamination of equipment, instruments is a virulent transmission vector from field into hospital
  - Wiping only sterilizes surfaces for an instant, no long term protection from contamination
- **Key technical approach: Permanent attachment of branching structure with antimicrobial tips**
  - Utilizing already-approved anti-microbial (AM) agents
  - PSIs use of branching attachment greatly increases the AM kill rate (50X)
  - Permanent attachment makes surfaces self-decontaminating
  - Wiping only needed to remove dead pathogens and dirt that cover the active surface
- **Minimal R&D effort required to apply technology to Air Force needs**
  - No new anti-microbial development
  - Only development is alteration of attachment chemistry to different surface types
  - Already demonstrated on stainless steel, aluminum, cotton, some plastics



Evacuation Litter: Coupon Production

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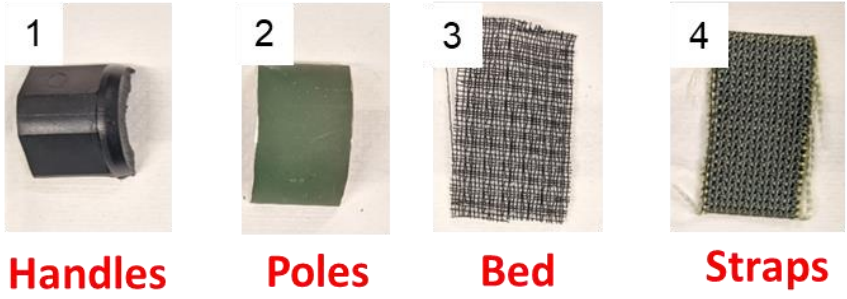
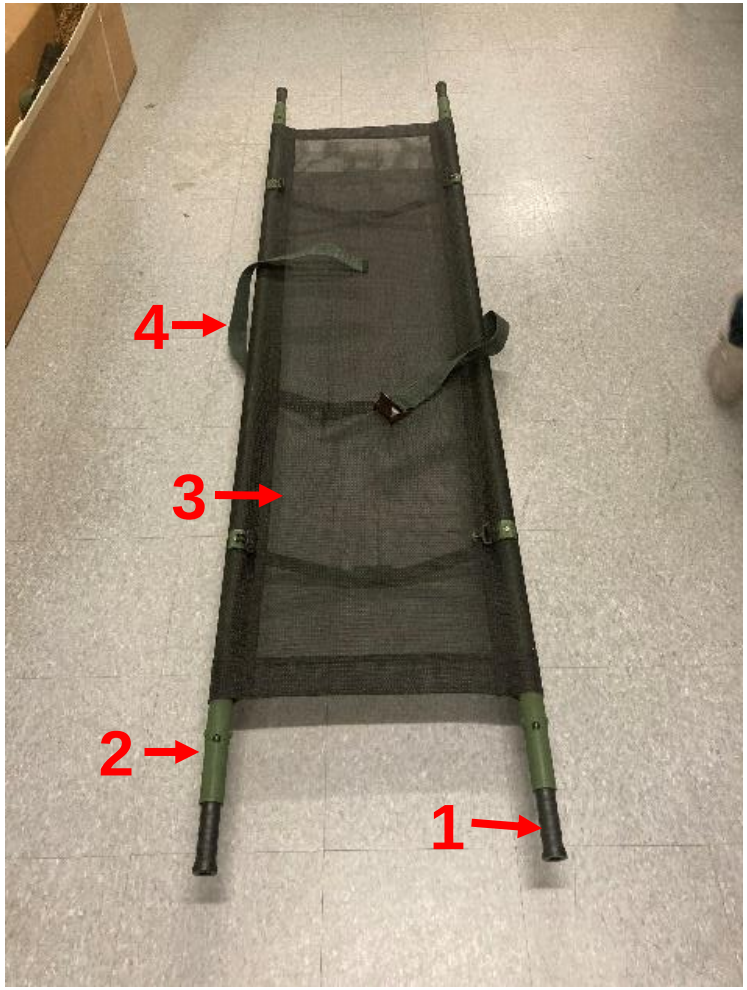
- **Generated coupons from multiple litter parts for evaluation of the antimicrobial coating. Based on the reported literature* the expected materials for various parts are:**
  - Handles: chemically resistant nylon
  - Poles: aluminum coated with polyurethane paint
  - Bed: polypropylene
  - Straps: polypropylene/nylon





** R. A. Castellani "Easily Decontaminated Stretcher" US5598592 (1997)*

Successfully generated coupons of representative surfaces (dimensions in the 1-2 in. range)

Blood Pressure Gauge: Coupon Production

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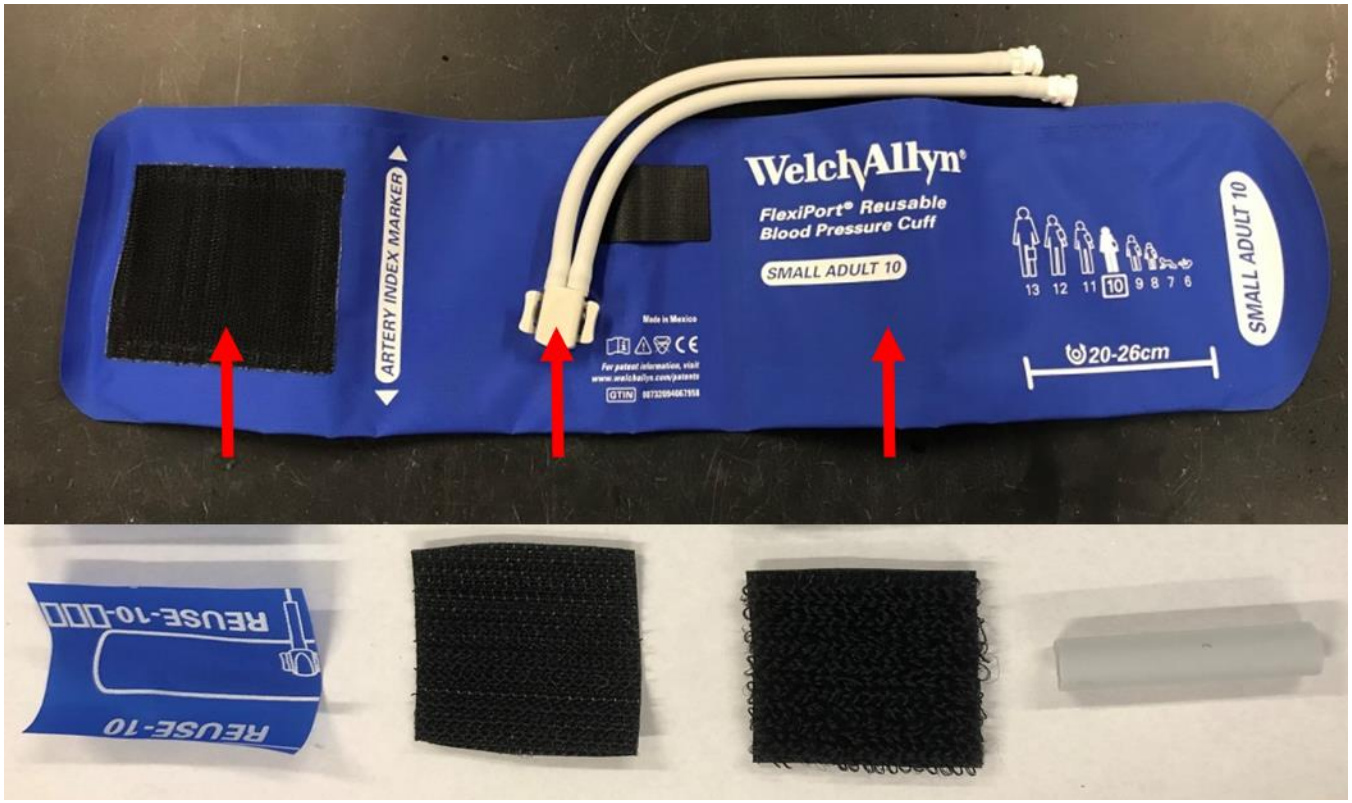
- **Generated coupons from multiple parts for evaluation of the antimicrobial coating. Based on the reported literature* the expected materials for various parts are:**
  - Fabric: Nylon
  - Velcro: Nylon & Polyester
  - Tubing: Silicone

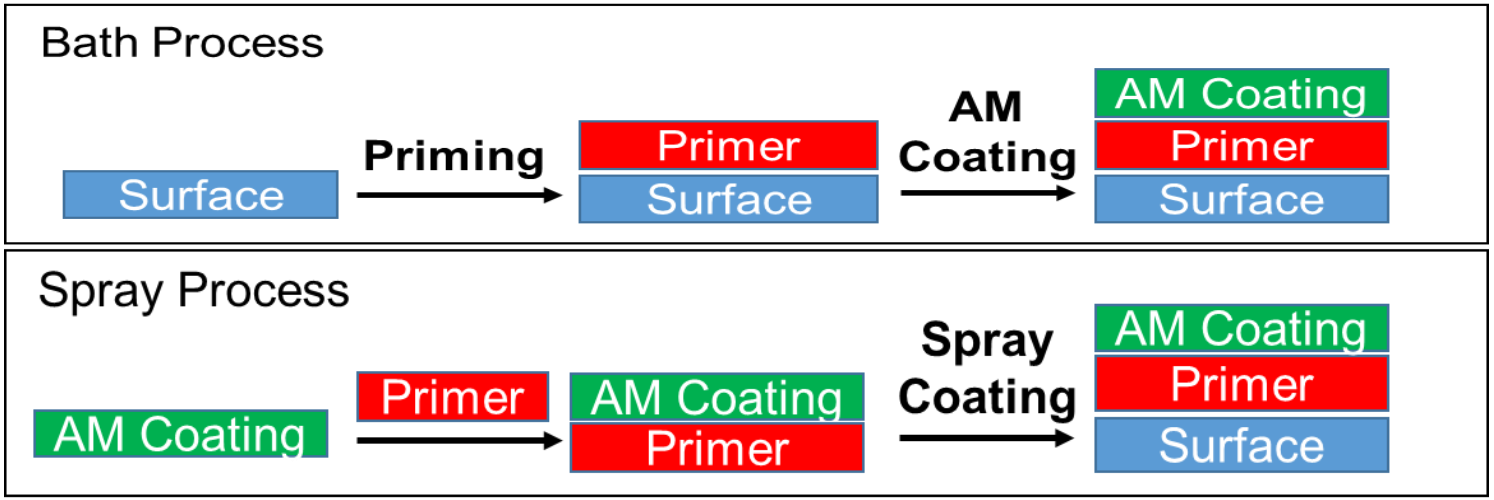


Fabric **Velcro Hook & Loop** **Tubing**

Successfully generated coupons of representative surfaces (dimensions in the 1-2 in. range)

AM Coating: Surface Application Processes

- **Litter & Blood Pressure Cuff surfaces have low concentrations of functional groups that can be used as attachment points**
  - Primer strategy evaluated
- **Procured and evaluated COTS primers for surface attachment efficacy**
  - Primers selected to prevent leaching based on literature precedent
- **Developed two distinct methods for application:**
  - Two step bath process (established methodology)
  - One step spray process (easier for repeat application)



Developed two unique coating methods for AM functionalization of various substrates

Surface Concentration Characterization

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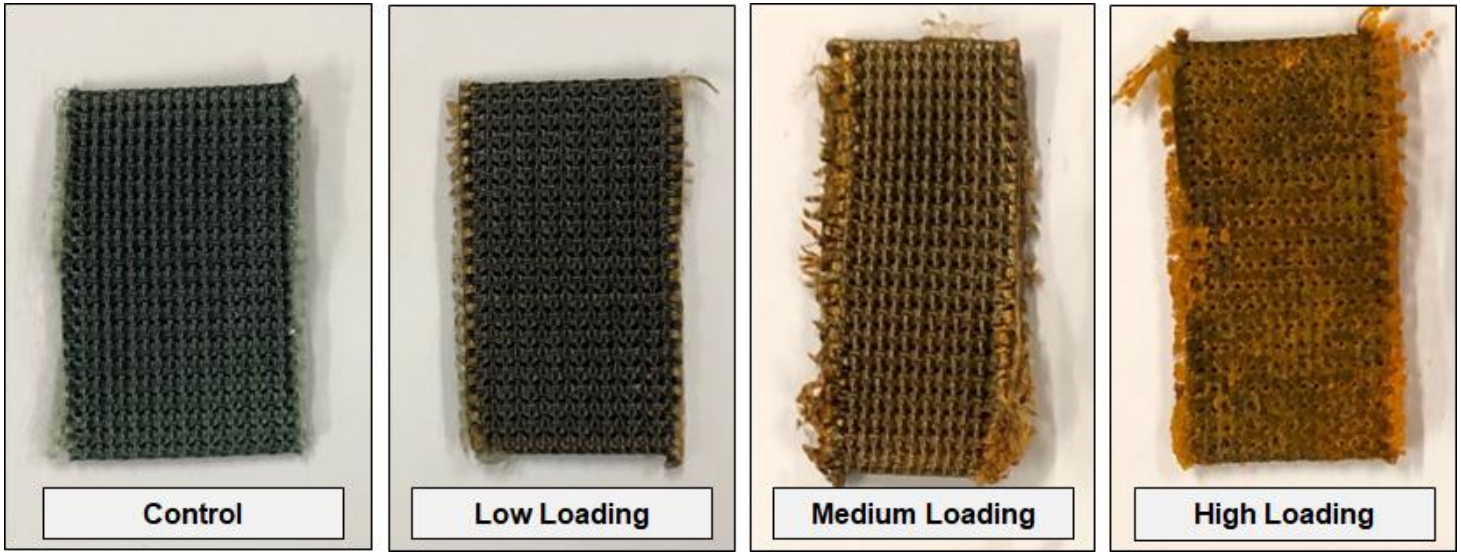
- **PSI developed colorimetric method to determine surface concentration of AM moiety**
- **Coating compound itself does not change visual appearance of the coupon**



Sample	Relative Surface Conc.
Control Fabric	0
Low Loading	1
Medium Loading	5x
High Loading	10x

PSI developed colorimetric determination method for AM surface concentration

AM Coating Provides Broad Spectrum Efficacy

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Pathogen Type	Name	% Kill
Viruses	***Sars-Cov-2***	**>99.9% *(99.999%)***
	VSV	**>99.9999% within 10 min.**
	MS2	99.95%
Surgical suite heater-cooler unit (HCU) bacteria	*M. Chimaera*	*>99.9999%*
Antibiotic resistant bacteria involved in healthcare-associated infections (HAI)	*MRSA*	*>99.99%*
	C. Difficile (vegetative)	>99.20%
	C. Difficile (spores)	>99.82%
Gram positive bacteria	*S. Aureus*	99.999%
	S. Epidermis	99.99%
Gram negative bacteria	*E. Coli*	99.99%
Fungus	*C. Albicans*	99.99%

2-6 log kill against viruses, bacteria, spores and fungi

Antiviral Evaluation - Background

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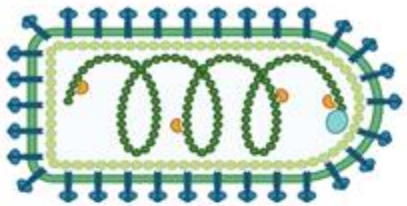


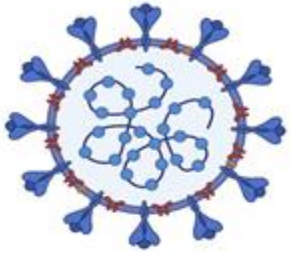
VSV

Negative Sense RNA Virus

BSL2

Full Molecular Toolbox

Fast Pace Testing



SARS-CoV-2

Positive Sense RNA Virus

BSL3

Minimal Molecular Toolbox

Slow Testing

VSV Virus is a good surrogate virus for rapid screening testing

Antiviral Evaluation – Experimental Procedure

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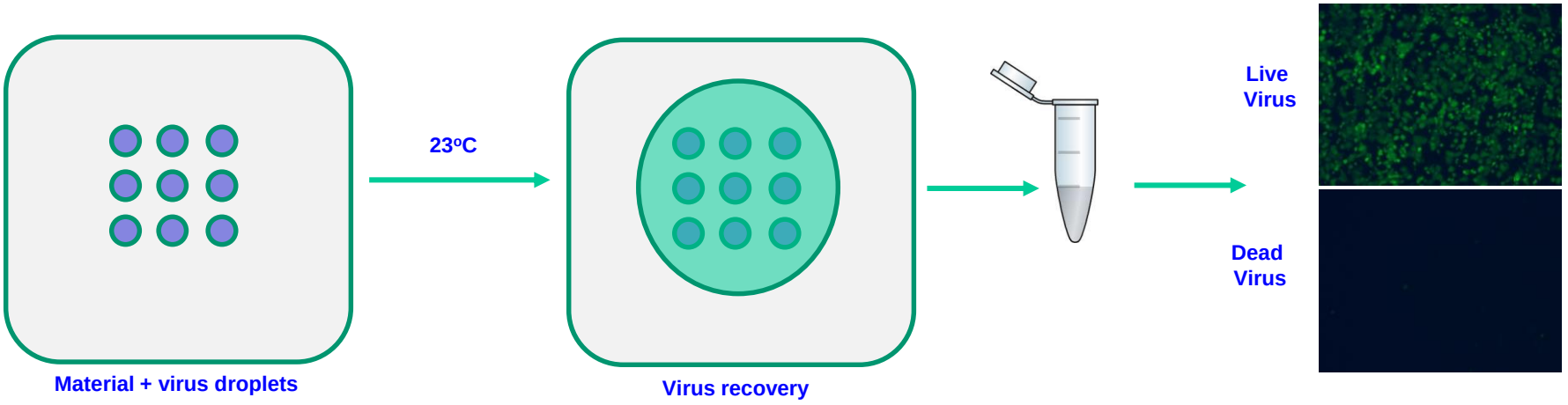
- Add virus to material in 3 x 3 grid of 2 uL droplets
- Allow virus to rest on treated or untreated surface for 30 mins at room temperature
- Recover virus with 1 mL of media
- Add recovered virus to healthy cells and look for CPE ~12 hours later using microscopy



Validated experimental procedure in place for antiviral screening

Antiviral Evaluation – Quantitation Methods

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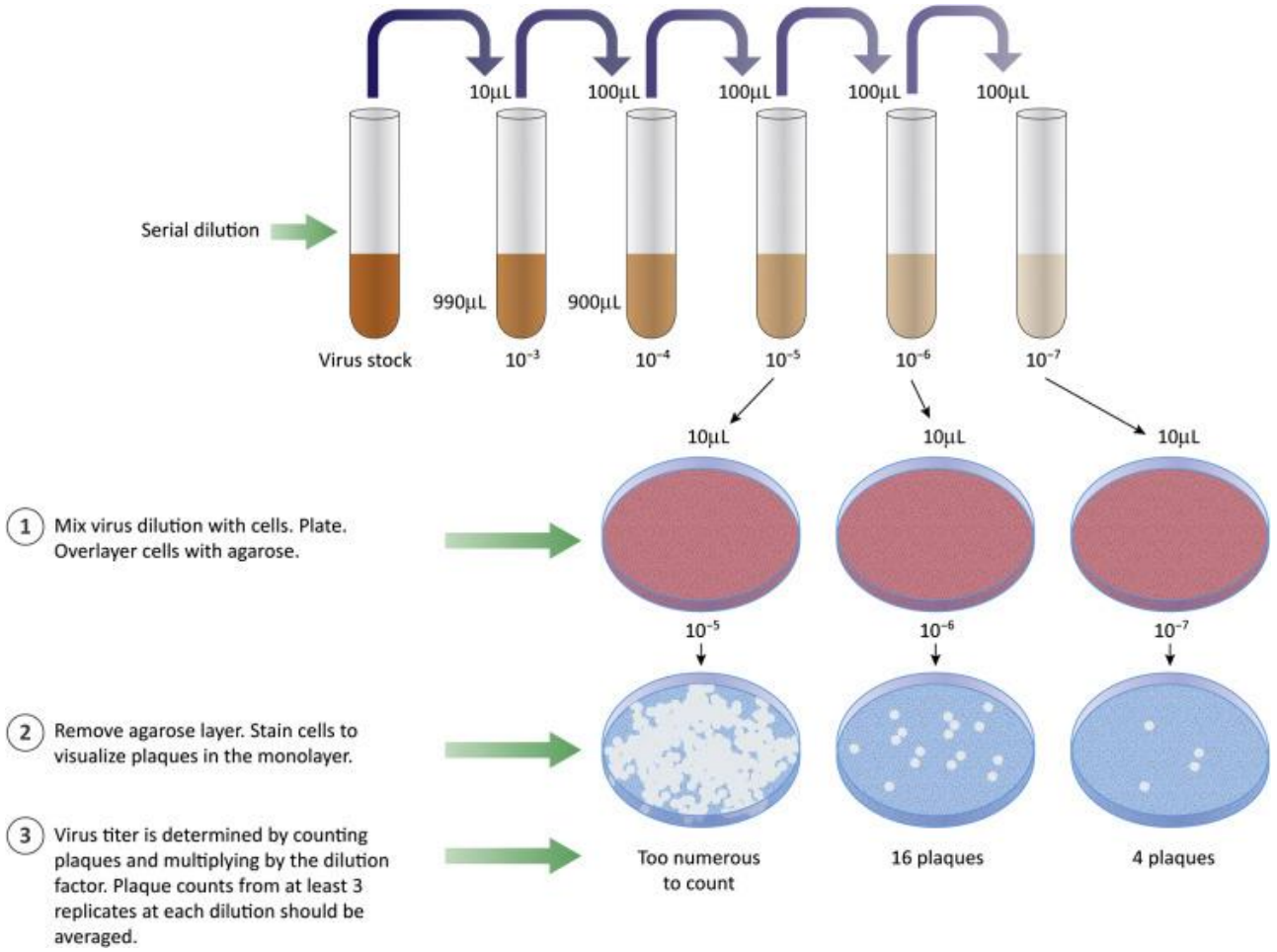
- **Plaque assay was used to quantify viral growth**



Validated experimental procedure in place for antiviral quantitation

Antiviral Testing

- **Hypothesis: AM coating will inhibit viral growth**

- **Methods: Use a known concentration of virus on treated and untreated surfaces and compare how recovered virus grows from each**
  - Quantify viral growth using microscopy and plaque assay

- **Prediction: If the AM compound is effective at inactivating virus, decreased viral growth will be observed in both microscopical analysis and plaque assay**

Antiviral Evaluation – VSV 10^7 PFU

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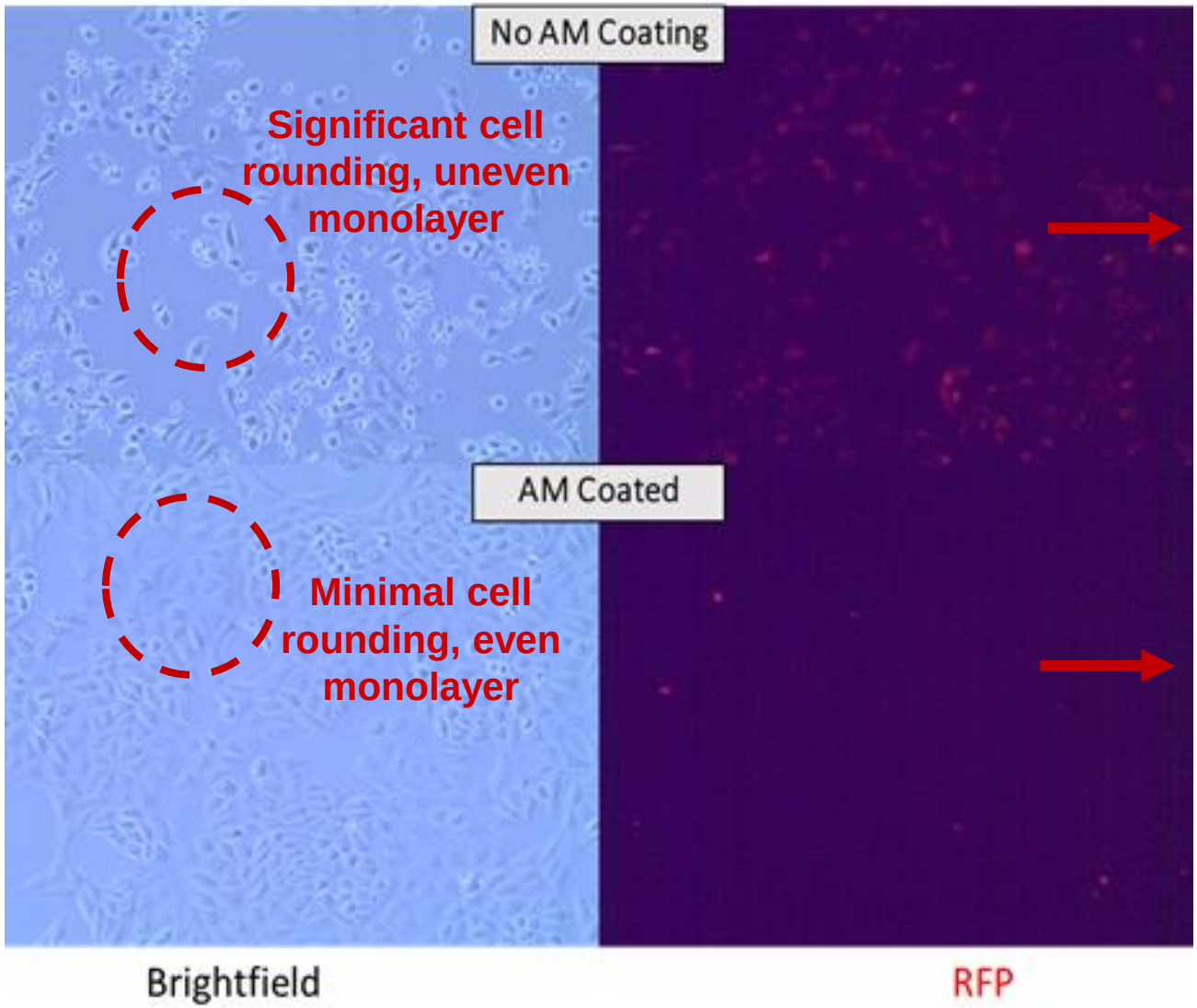
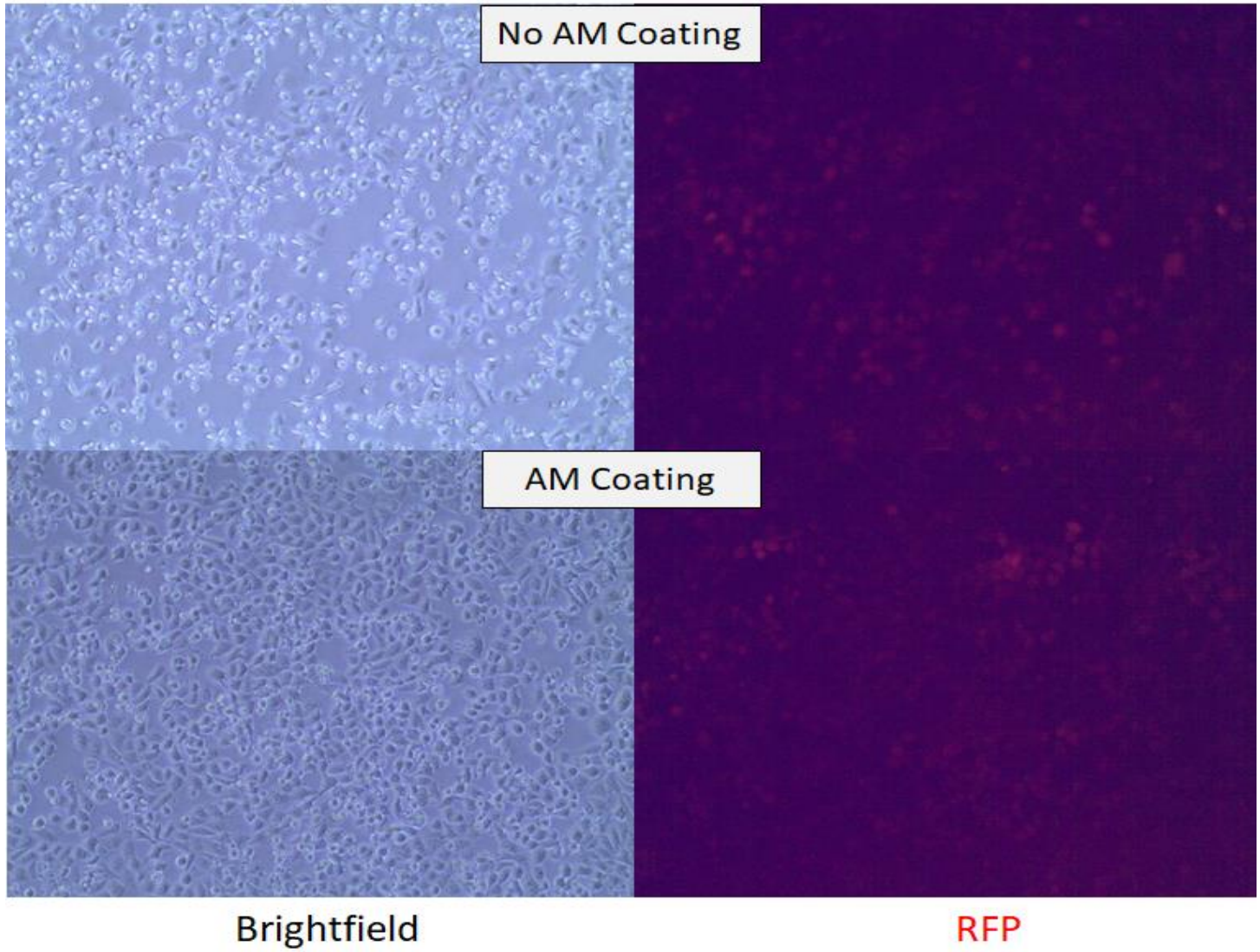


AM coating causes significant viral reduction on metal surfaces

Antiviral Evaluation – VSV 10^7 PFU



AM coating causes significant viral reduction on fabric surfaces

Antiviral Evaluation – VSV 10^7 PFU

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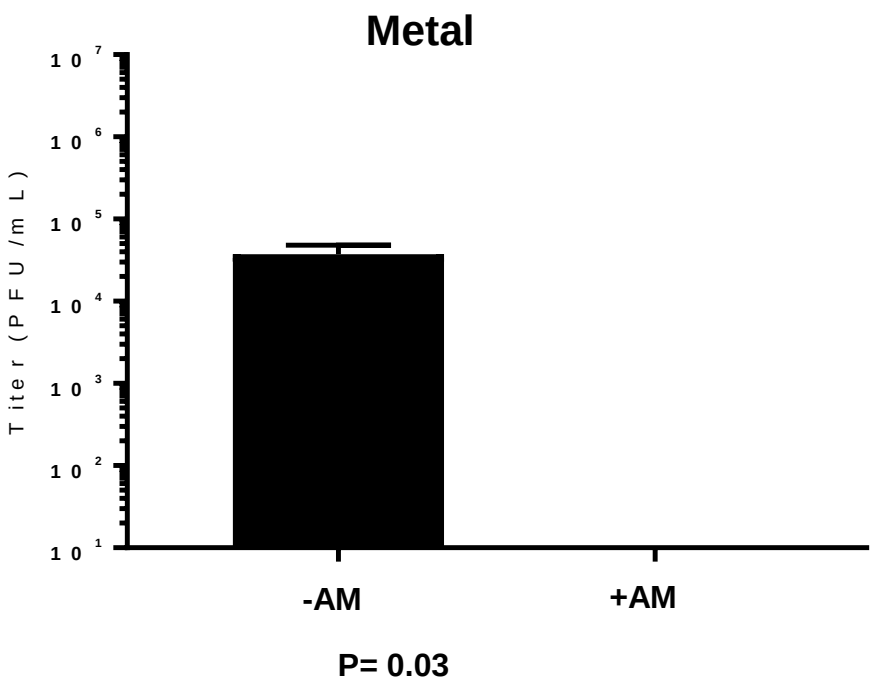

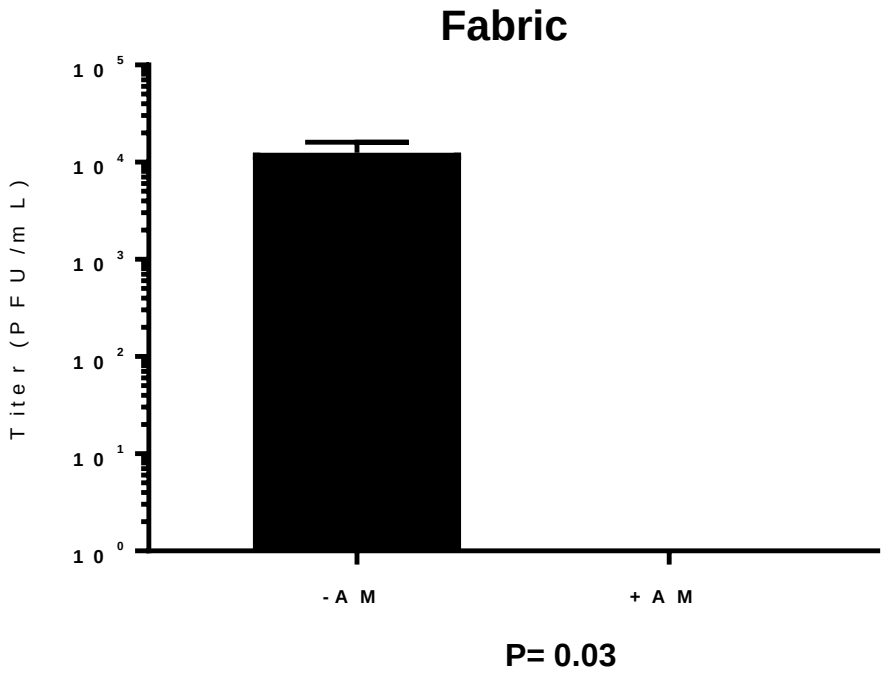

Material	Log Reduction
Metal	>4.6
Fabric	>4

AM coating shows high antiviral activity in metal and fabric surfaces

Antiviral Evaluation – VSV 10^7 PFU

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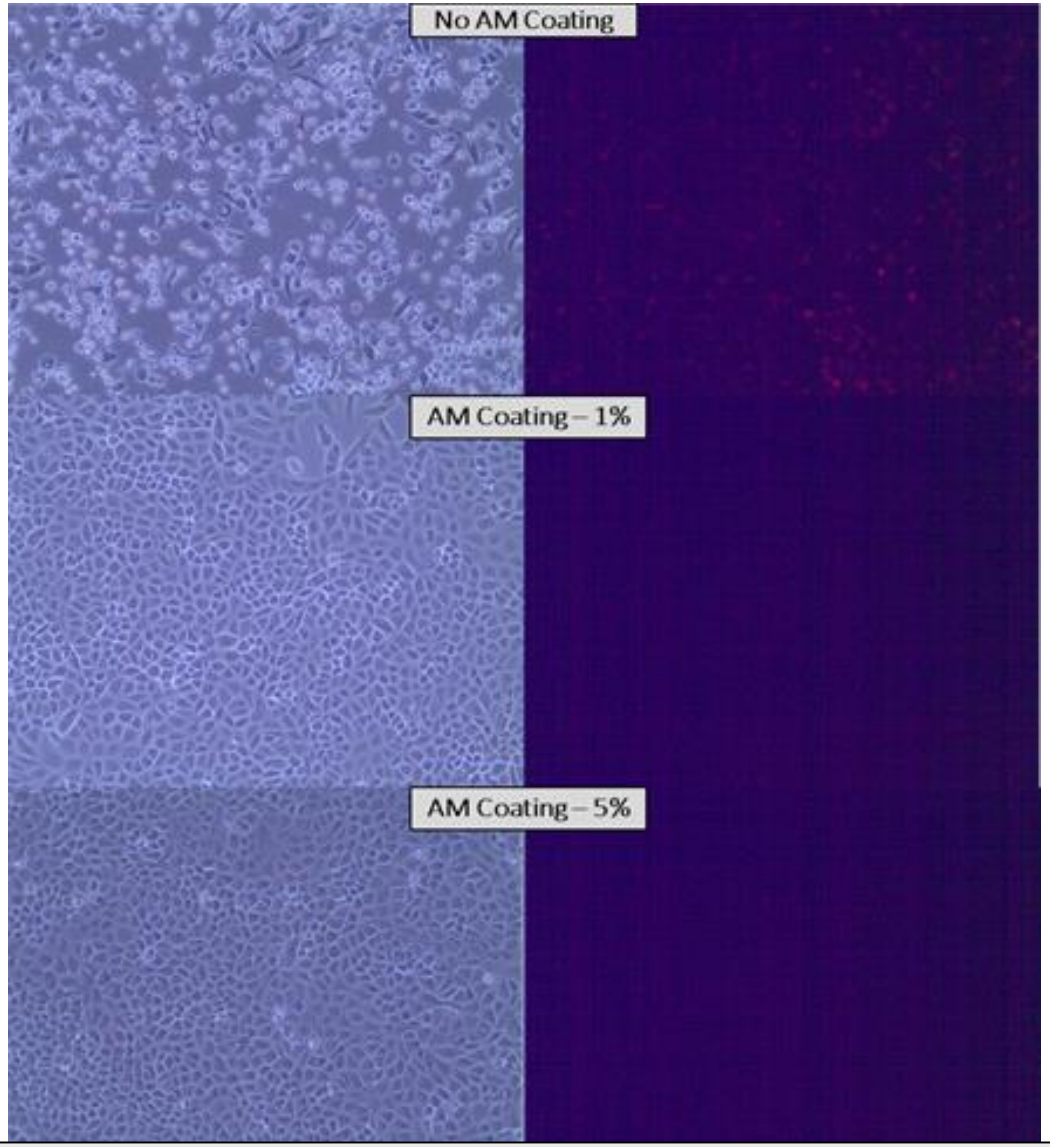
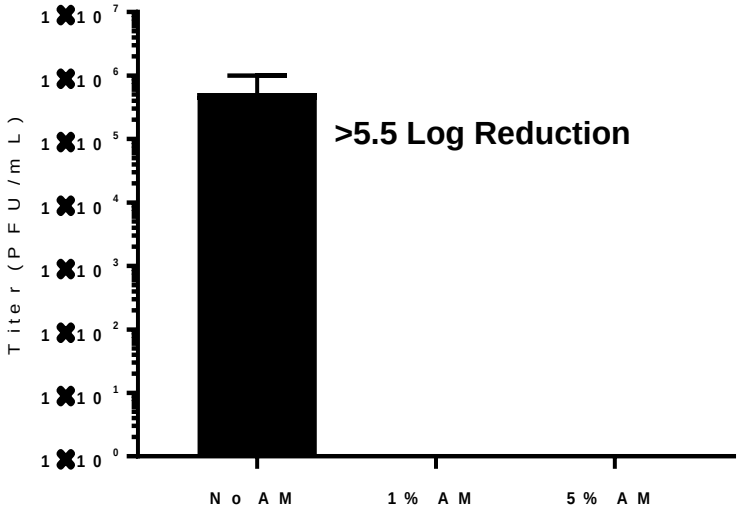
Blood Pressure Cuff Fabric



- **Evaluation of AM spray concentrations effect on viral efficacy**



Increased surface loading yielded undetectable viral titer via microscopy or viral titer

Antiviral Evaluation – Varying PFU Concentration

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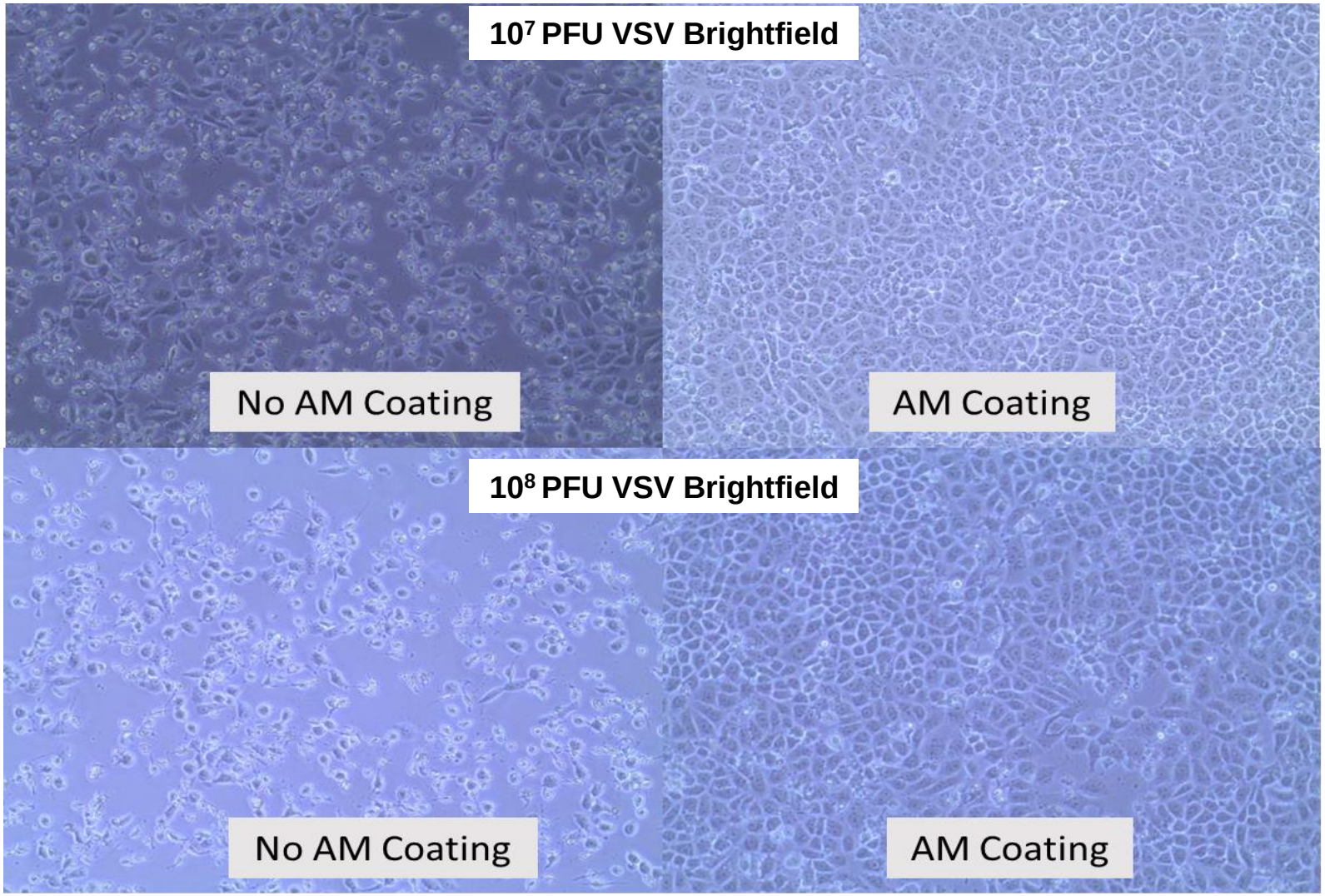

AM Coating is effective at eliminating viral load at concentrations of 10^8 PFU

Antiviral Time Course Testing - VSV

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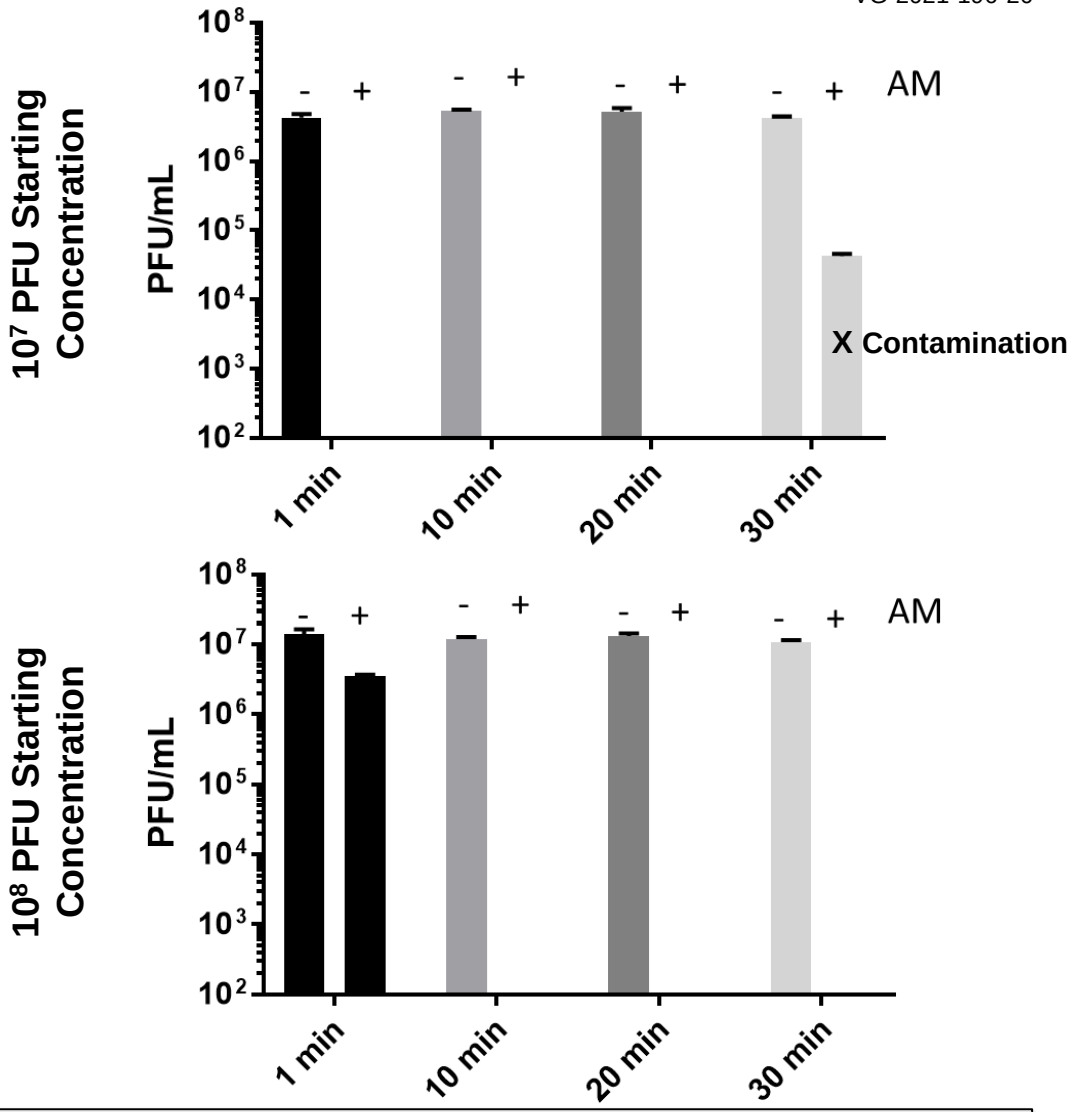
- **Time course testing was conducted to determine AM coating kill half life against VSV virus at varying time points**
  - **1, 10, 20, 30 min time points tested**
- **AM coating demonstrated AM efficacy at <10min inoculation time for both 10^7 and 10^8 PFU**



AM coating rapidly decontaminates viral load from coated test articles

Surface Loading VS Efficacy

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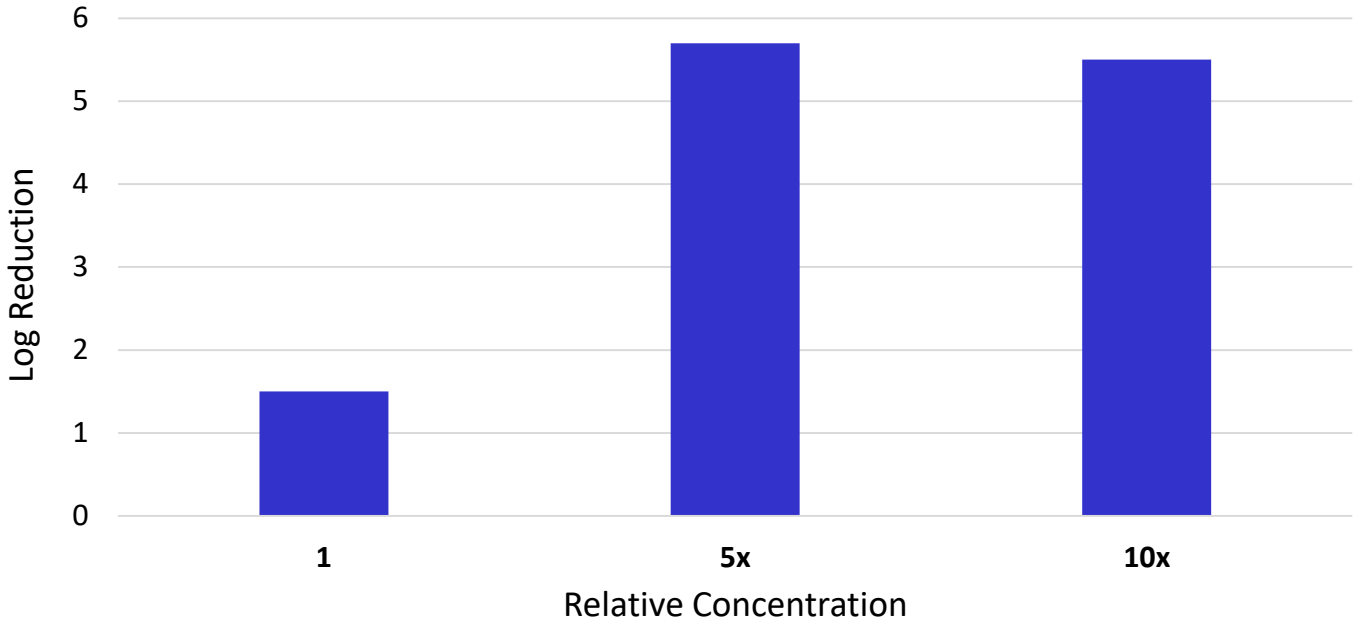

Sample ID	Relative AM Surface Concentration	AV Efficacy (Log Reduction)	AV Efficacy (% Reduction)
Low Loading	1	1.5 Log Reduction	96.9
Medium Loading	5x	>5.5 Log Reduction	99.9999
High Loading	10x	>5.5 Log Reduction	99.9999

Trends indicate increasing AM concentration leads to higher antiviral efficacy

Antiviral Evaluation – SARS-CoV-2 - 10^7 PFU

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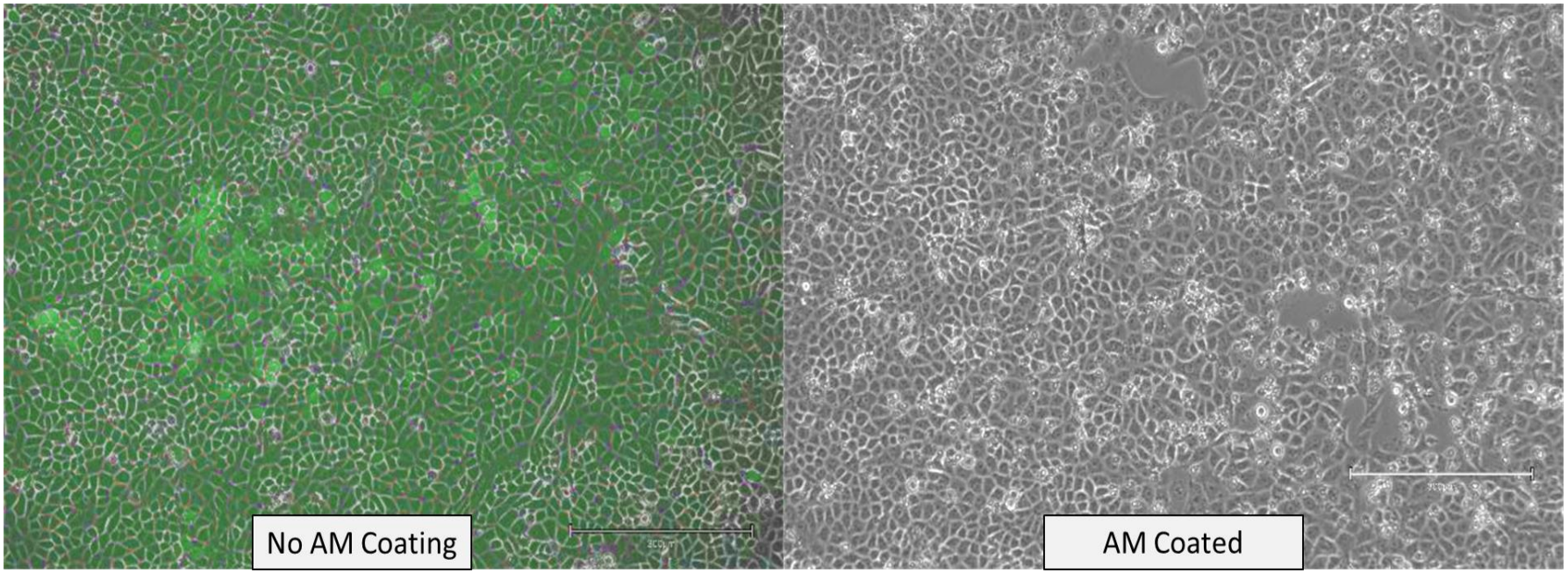
- **SARS-CoV-2 Neon used for testing**
  - Washington Isolate paired with green fluorescent marker
  - Green fluorescence indicates active virus
- **Testing was conducted in triplicate for statistical significance**



- **Quantitative plaque assays show 100% reduction in viral growth**

PSI AM coating reduced SARS-CoV-2 below the limit of detection

Conclusions

- **Successful production and evaluation of antimicrobial (AM) surfaces**
  - Produced AM material to coat 1000 m^2 of surfaces
    - Developed colorimetric method to quantify AM surface loadings
  - Produced coupons of representative surfaces of evacuation litter & blood pressure cuff and successfully developed methodologies for AM coating with high surface loadings
  - Demonstrated antimicrobial activity for all surfaces (as high as >6 log reduction)
    - *VSV Virus*: >4 Log reduction for all relevant materials
      - Kill half-life <10 min.
    - *SARS-CoV-2* → Reduction of viral activity below limit of detection
      - Initial testing indicates >3(5) Log reduction
  - Correlated AM surface loading with antimicrobial efficacy
- **Next Steps:**
  - Evaluate coating robustness to operational wear to demonstrate efficacy during the service life

Acknowledgements

Air Force Team:

- COTR: Mr. Ric Stefanski (AMC)
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- Mr. Victor de Leon (ACC)
- Dr. Amber Malory (AETC)
- Lt. Col. Todd Roman (AMC)

Abstract

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Abstract: The Air Force has identified an urgent need to reduce COVID-19 contaminant loads in environments where Airmen operate (e.g., patient transfer mobility aircraft) and thus decrease transmission likelihood. Physical Sciences Inc. (PSI) and National Emerging Infectious Disease Laboratories at Boston University (NEIDL/BU) are developing an antimicrobial coating and demonstrate its effectiveness on evacuation litter products and blood pressure monitoring equipment. PSI is coating multiple medical equipment materials with a permanently attached, broad-spectrum antimicrobial technology. The coating was previously demonstrated on textile, metal and plastic surfaces for strong attachment and broad spectrum antimicrobial activity against bacteria, spores, fungi and viruses. The coating efficacy for the target surfaces is being demonstrated against a virus panel and other pathogens of interest. The coating is being optimized to achieve high levels of viral reduction within a short amount of time. The robustness of coating in litter operation is being evaluated upon weathering, abrasion, and cleaning. The coating was developed based on prior PSI studies that demonstrated broad spectrum antimicrobial activity of fabric and metal surfaces against bacteria, spores, fungi and viruses. Greater than 99-99.999% kill efficiency was demonstrated against: (a) antibiotic-resistant bacteria: *C. Diff.* (both vegetative cells and spores), *MRSA*, (b) sterilization resistant spores (*Bacillus, sp.*), (c) clean room bacteria (*B. atrophaeus*), (d) Gram-positive bacteria (*S. Aureus, S. Epidermis*), (e) Gram-negative bacteria (*E.Coli*), (f) fungus (*C. Albicans*) and (g) non-enveloped viruses (*MS2*). Biocompatibility of fabric coupons was also demonstrated with no cytotoxicity or skin irritation. Results to date indicate strong attachment of the antimicrobial coating to surfaces of NATO evacuation litter and blood pressure cuff materials. The coating process was optimized to provide uniform and high-density coverage across all materials. Formulations for both bath and spray coating processes have been developed. All coated materials showed antiviral activity high efficacy (up to 5.5-log reduction, >99.999% kill efficiency) against a COVID-19 surrogate, Vesicular stomatitis virus (VSV). The antiviral efficacy was demonstrated by qualitative microscopy/imaging experiments as well as by quantitative plague forming assays. Various surfaces including litter bedding, litter poles, litter handles, litter straps and blood pressure cuff fabrics were demonstrated for antiviral activity with high efficacy.