The Use of Antimicrobials in Silicone Materials for Healthcare Products

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Minneapolis, MN
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Betsy D. Carlton, PhD DABT
Agenda

- Introduction
- About Antimicrobial Silicones
- Factors to Consider When Selecting an Antimicrobial Silicone Solution
- Bluestar’s Approach
Bluestar Silicones: At a Glance

Strength of the Mineral (Si)
Creativity of the World of Organics (O)

Key Figures
- WW Operations Lyon, France
- Sales $626 Million
- Employees >2,000
- Production Sites 10
- R&D Budget 4.5% of sales
Silicones are ideal for medical applications for physical properties, functionality and biocompatibility.
About Antimicrobials
What does “Antimicrobial” mean?

- “destroying or inhibiting the growth of microorganisms and especially pathogenic microorganisms.”

Why the Need for Antimicrobial Silicones?

- Spread of hospital acquired infections (HAI) and increases in HAI-related mortality cases
- Effective January 2012, Medicare no longer reimburses hospitals for preventable HAI infections
- Development of antibiotic resistant pathogenic strains
- Improved Hygiene and Odor Reduction
- Mildew Prevention

Consumer interest in the products with embedded anti-microbial properties
The High Cost of Hospital Acquired Infections

Annual direct medical costs of Hospital Acquired Infections (HAI) to U.S. hospitals are estimated to range from $28.4 to $33.8 Billion, and from $36 to $45 Billion for inpatient services\(^1\)

- Estimates of the most common HAIs per year include approximately 450,000 cases of catheter-associated urinary tract infections, 290,000 surgical site infections; 178,000 Clostridium difficile (C-diff) infections, 180,000 central line blood stream infections and 53,000 ventilator-associated cases of pneumonia

- Cost-savings benefits of infection prevention for these HAIs range from $5.7 to $31.5 Billion on an annual basis

- Use of antimicrobial devices are included among the arsenal of infection-control strategies recommended by the US CDC\(^2\)

\(^1\) [http://www.cdc.gov/HAI/burden.html](http://www.cdc.gov/HAI/burden.html)
\(^2\) [http://www.cdc.gov/hicpac/CAUTI_fastFacts.html](http://www.cdc.gov/hicpac/CAUTI_fastFacts.html)
Types of Antimicrobial Additives

Microbicidal/microbiostatic additives may have

- Multiple sites of action
  - **Inorganic**
    - Micro/nano particle metals, metal oxides; silver is most commonly used
    - Zeolites (aluminosilicate)
    - Glasses
  - **Organic**
    - Heterocycles
    - Aromatic Compounds
    - Other classes

- Or a single site of action
  - Antibiotics
  - Antifungals
  - Antivirals
Antimicrobial properties can be achieved by modifying surface or bulk silicones.
Bacteria (Streptococcus mutans MT8148) adhered to (a) an untreated Ti surface, while bacterial adhesion was inhibited on (b) a PEG-electrodeposited Ti surface.

Hanawa T J. R. Soc. Interface 2009;6:S361-S369
With permission from The Royal Society and author

Advantages:
- small quantity of material used
- no effect on mechanical properties of bulk

Drawbacks:
- additional processing step
- tight processing conditions to achieve uniformity
- subject to damage/scratch/removal

www.sharklet.com

S. aureus after 14 days
Bulk Modification of Uncured Material

Advantages:
- No additional manufacturing steps needed (cost savings)
- Not affected by surface damage
- Prolonged release

Drawbacks:
- Larger quantity of additive needed
- May have effect on bulk material properties
Bulk Modification of Cured Material

Soaking of the article in solution of antimicrobial

Advantages:
- Ability to incorporate unstable antimicrobial additives

Drawbacks:
- Additional complex manufacturing steps required
Factors to Consider When Selecting an Antimicrobial Solution
A Variety of Factors Need to be Considered

- What is your application?
  - FDA or EPA regulated?

- What silicone?
  - LSR, HCR, RTV, Gels

- What key physical properties must be achieved?

- What bacteria are you trying to control?
  - What is your targeted log reduction?

- What claims do you want to make when placing product on the market?

- How long is the activity needed?

- Is the material pigmented or do you require transparency?

- What testing do you require?
  - How will you determine efficacy/quality control?

- What does the part get exposed to after it is made?
Factors to Consider…

What is your Application and What Claims Do you Intend to Make?
1000s of antimicrobial products using a wide range of antimicrobial additives are regulated by EPA or FDA.

Skin Contact Applications with Antimicrobial Additives are Regulated by EPA

- Phone and I-pod cases
- Keyboards
- Computer mouse
- Touch screens
- Door knobs
- Elevator buttons
- Shoe inserts
- Prosthetic liners

Medical Device Applications are Regulated by FDA

- Needle-free connectors
- Urinary catheters
- Central venous catheters
- Instrument handles
- Urinary collector plugs
- Wound dressings
- Mattress covers
- Prosthetic liners
Type of medical claims for products with antimicrobial properties

You MUST be able to substantiate your antimicrobial claims

**Type of claims:**
- Medical devices
- Claims toward specific pathogenic bacteria
- Claims preventing or curing disease or infection

**Type of claims:**
- Containing additives to prevent destruction of the material by bacteria
- Odor control
- Prevention of the bacterial growth on the surface of material
### Examples of EPA fines for Failure to Register or Unsubstantiated Claims

<table>
<thead>
<tr>
<th>Year</th>
<th>Company name</th>
<th>Product and claims</th>
<th>Fine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>VF Outdoor, Inc.</td>
<td>60 shoe products</td>
<td>$207,500</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“antimicrobial protection” and inhibiting the growth of “disease-causing bacteria”</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Crocs, Inc.</td>
<td>Shoes</td>
<td>$230,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>antimicrobial claims</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>Califone International, Inc.</td>
<td>Headphones</td>
<td>$220,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“prevent the spread of bacteria, mold and mildew for student protection.”</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>ATEN Technology, Inc.</td>
<td>Wireless laser mouse with nano-shield coating, products’ abilities to control germs and pathogens</td>
<td>$208,000</td>
</tr>
<tr>
<td>2007</td>
<td>Target</td>
<td>Toilet Seats, Mattresses, and Pillows</td>
<td>$40,950</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“germ-killing” claims</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>Kmart</td>
<td>Garden Hoses</td>
<td>$110,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>inhibit mold, fungus, and bacteria growth</td>
<td></td>
</tr>
</tbody>
</table>
Factors to Consider…

What are you trying to kill?
Different types of infective agents create different problems to be solved

- Low bacterial counts may grow to present significant colonization of the product surface very quickly
- Increasing number of antibiotic-resistant bacteria such as methicillin-resistant Staph aureus (MRSA)
- Gram negative bacteria (E. coli, P. aurigenosa) may respond to different antibiotics than do gram positive bacteria (S. aureus)
- Biofilm (colonies of cells that stick to each other on a surface, embedded within a self-produced matrix of extracellular polymeric substance) acts as a barrier to antimicrobials reaching the target organism
- Fungi such as Candida albicans and viruses do not respond to antibiotics, but rather require other antimicrobial treatments
Antimicrobial efficiency is not equal across the spectrum

ISO 22196 test procedure. Concentration of antimicrobial additives in silicone is the same for both additives

When selecting an antimicrobial additive, the OEM needs to determine the targeted bacteria, log reduction and longevity of activity.
Factors to Consider...

Desired Mechanical Properties
Antimicrobial Additive Can Affect Mechanical Properties

Mechanical properties of material with antimicrobial additive

- Reinforcement
- Plasticization

Depending upon the interaction, final properties of the silicone can improve or deteriorate
Selected Antimicrobial and Concentration Levels can have a Major Impact on Properties
Factors to Consider…

Manufacturing Process
Manufacturing Considerations

- **Factors Ensuring Performance:**
  - Adequate Mixing
  - Precise Dosage

- **Contamination Prevention:**
  - Separate equipment
  - Cleaning of equipment

- **Quality Control:**
  - Quantitative analysis
  - Performance analysis
  - Uniformity of distribution of the antimicrobial additive in the sample
Effect on cure speed of material

- Antimicrobial additives may have reactive functional groups
- Silicone material network formation includes chemical reaction *in-situ*
- Presence of “foreign functional groups” may interfere with the cure reaction of silicone:

**Polycondensation mechanism**
- little or no effect

**Hydrosilation mechanism**
- possibility of cure retardation due to Pt catalyst poisoning

**Radical polymerization mechanism**
- Interaction with propagating radical affects chain length and crosslink density
Antimicrobial Additive Can Impact Cure Speed Affecting Cycle Time and Productivity

Time needed to achieve 90% cure of the material

Measurement taken at 240°F. Efficiency for all samples – 99.99% reduction of S. aureus (ISO 22196)

Cure speed measured by Moving Disk Rheometer.
Temperature of Molding and Sterilization Need to be Adjusted Based on Antimicrobial Additive

Additive 1 stable over wide range of temperatures

Additive 2 decomposes at 160°C

Average molding temperature 115° to 200°C

For Additive 2 molding temperature has to be adjusted to prevent additive decomposition
Process Conditions May Need to be Adjusted to Accommodate Changes in Rheology

- Changes in rheology will affect fill of the mold, which can lead to defects
- Shrinkage value important for complex parts. If different than incumbent, may affect assembly.
Select Antimicrobial Additives may Shorten Shelf-life of the Un-Cured Silicone Material

Max Torque in moving disk rheometer experiment is correlated with mechanical properties of the material.

Conditions such as Cure Speed, Mechanical Properties, Rheology can be adjusted by changes in formulation of the silicone material itself and via the method of antimicrobial additive incorporation.
Factors to Consider…

Desired Aesthetics
Addition of Antimicrobial May Impact Appearance of the Device

- **Cured silicone:**
  - transparent and colorless
  - un-reacted silicone hydride Si-H (reduction)

- **Addition of antimicrobial additive:**
  - May change color due to additive color
  - May change color due to chemical reactions of antimicrobial additive
A Change in Color May Happen over Time with Select Antimicrobial Additives

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Permeability<em>10^9, cm^3</em>cm/(s<em>cm^2</em>cmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethylsilicone rubber</td>
<td>60.0</td>
</tr>
<tr>
<td>Fluorosilicone</td>
<td>11.0</td>
</tr>
<tr>
<td>Nitrile rubber</td>
<td>8.5</td>
</tr>
<tr>
<td>Natural rubber</td>
<td>2.4</td>
</tr>
<tr>
<td>Polyethylene, low density</td>
<td>0.8</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>0.12</td>
</tr>
<tr>
<td>Polyethylene, high density</td>
<td>0.10</td>
</tr>
<tr>
<td>Nylon 6</td>
<td>0.004</td>
</tr>
<tr>
<td>Poly(ethylene terephthalate)</td>
<td>0.0019</td>
</tr>
<tr>
<td>“Teflon”</td>
<td>0.0004</td>
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</tbody>
</table>

Highly permeable material + oxidation/reduction of additive = Change in color with time

In Summary, each Antimicrobial can have a Different Interactive effect with the Silicone

<table>
<thead>
<tr>
<th>Additive</th>
<th>Mechanical</th>
<th>Cure</th>
<th>Optical, act. color</th>
<th>Efficiency</th>
<th>Dispersion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td>yellow-opq</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td>white</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
<td>yellow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
<td>transp-opq.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td></td>
<td></td>
<td>khaki</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td>khaki</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td></td>
<td></td>
<td>green-gray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td></td>
<td></td>
<td>transp</td>
<td></td>
<td></td>
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<tr>
<td>I</td>
<td></td>
<td></td>
<td>transp</td>
<td></td>
<td></td>
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<tr>
<td>J</td>
<td></td>
<td></td>
<td>transp-opq.</td>
<td></td>
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<tr>
<td>K</td>
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<td></td>
<td>transp-opq.</td>
<td></td>
<td></td>
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<tr>
<td>L</td>
<td></td>
<td></td>
<td>transparent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td></td>
<td></td>
<td>opq-white</td>
<td></td>
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</tbody>
</table>
Customer needs are very specific to the application and vary for each case. Bluestar understands that there is no “one size fits all” solution and takes custom tailored approach to meet the antimicrobial requirements of the customers.

Bluestar has built the library of the antimicrobial additives that are compatible with silicone material and is not limited to one antimicrobial.

Combined knowledge of the effect of the antimicrobial additives on the silicone properties and technical knowledge of the silicone technology gives us ability to best fit customer needs with the antimicrobial solution.

Bluestar performs matching of the antimicrobial additives to efficacy needed based on ISO 22196 or other tests.
Bluestar Example Case:

THE TARGET
- High efficacy against bacteria
- Little-to-no impact on mechanical properties (in-spec hardness and elongation)
- No impact on cure kinetics
- Product appearance – hazy white

THE RESULTS

<table>
<thead>
<tr>
<th></th>
<th>Log Reduction of the microorganism count vs control (Planctonic/Biofilm)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E.coli</td>
</tr>
<tr>
<td>Bluestar HCR 65 durometer with antimicrobial additive</td>
<td>7.7 / 3.6</td>
</tr>
</tbody>
</table>

*test developed by Microban
What will make this path successful?

Collaboration = Success

**OEM**
Product Requirements Definition

**Molder/OEM**
Processing Expertise

**Testing Facility**
Efficiency Expertise

**Material Supplier**
Silicone Expertise
Antimicrobial Interaction
THANK YOU!
Helpful resources

http://www.cdc.gov/hicpac/CAUTI_fastFacts.html

http://www.cdc.gov/HAI/burden.html


http://www.cdph.ca.gov/programs/Biomonitoring/Pages/default.aspx

http://www.epa.gov/pesticides/factsheets/treatart.htm

http://www.epa.gov/pesticides/bluebook/

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071380.htm