Antimicrobial Polymers in Medical Devices As Part of the Fight Against Healthcare-Acquired Infections (HAIs)

Design Considerations for Use of Homogenous Antimicrobial Materials
Executive Summary

Select elastomers with specific antimicrobial additives have shown excellent antimicrobial efficacy and biocompatibility while maintaining much of their mechanical properties and processing capabilities. To help reduce the spread of hospital-acquired infections, medical device manufacturers can engineer antimicrobial properties directly into their devices.

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The Challenges of Healthcare-Acquired Infections

On February 8, 2006, President George W. Bush signed the Deficit Reduction Act (DRA) of 2005. Section 5001(c) of DRA requires: “…the Secretary to identify conditions that…could reasonably have been prevented through the application of evidence-based guidelines…” and that “…after October 1, 2008, hospitals will not receive additional payment for cases in which one of the selected conditions was not present on admission.”

The U.S. government was spurred into action due to the enormous costs — in both dollars and lives — inflicted by Hospital-Acquired Infections (HAIs):

- 4% of patients (721,800) in acute care hospitals infected, with 75,000 deaths/year (2011 estimates from the CDC — Centers for Disease Control and Prevention)
- $28 to $45B/year in healthcare cost (2009 CDC estimate)

Sources of HAIs

From The New England Journal of Medicine, March 27, 2014:

Device-associated infections (i.e., ventilator-associated pneumonia, catheter-associated urinary tract infection and central-catheter-associated bloodstream infection) accounted for 25.6% of all healthcare-associated infections; together, device-associated infections and surgical-site infections (21.8%) accounted for 47.4% of all healthcare-associated infections...

According to the CDC, specific sources of device-associated infections in acute care hospitals are:

- Catheter-Associated Urinary Tract Infection (UTI or CAUTI): 54,500 (estimate for 2012)
- Central Line-Associated Bloodstream Infection (BSI or CLABSI): 30,100 (estimate for 2012)
- Ventilator-Associated Pneumonia (VAP) in non-neonatal intensive care units: 49,900 (estimate for 2011)

Surgical site infections (SSIs)

from inpatient surgeries were estimated as 157,500 for 2011.

A partial list of hospital-onset pathogens, including drug-resistant microbes:

- Clostridium difficile
- Staphylococcus aureus, including methicillin-resistant (MRSA), which accounts for 55% of HAIs, and vancomycin-resistant S. aureus
- Klebsiella pneumoniae or K. oxytoca
- Escherichia coli
- Vancomycin-resistant Enterococcus
- Carbapenem-resistant Enterobacteriaceae (CRE), which is resistant to nearly all antibiotics available
- C. albicans
- Aspergillus niger
- Acinetobacter baumannii (75% are multidrug resistant)
- Pseudomonas aeruginosa (17% are multidrug resistant)

As the director of the CDC, Dr. Tom Frieden, stated in 2013, “If we’re not careful, we will soon be in a post-antibiotic era. And, in fact, for some patients and some microbes, we are already there.”

In addition to hospital-acquired infections, microbes can cause medical devices to have biofilm/biofouling, microbial odor, staining and discoloration and lose mechanical and physical properties due to microbial degradation.
CDC Recommendations for Medical Device Manufacturers

In response to the above challenges, U.S.A. government agencies and clinical organizations have issued recommendations and best practices to prevent infections acquired within a hospital environment. However, healthcare providers are facing great financial pressures—as well as labor shortages—making change in employee practices difficult to implement and sustain.

For example, the CDC reports that only 30% to 38% of U.S. hospitals are in full compliance with the CDC’s current infection control guidelines.5

Among the current top CDC recommendations to prevent healthcare-associated infections is the use of antimicrobial impregnated catheters and cuffs.9 Antimicrobial polymers have numerous additional potential uses for reducing risks of HAI, including specific application requirements in:

- Vascular Access Devices: Catheters, Injection Systems, Needleless Connectors, etc.
- Fluid Management Devices: IV Systems & Bags, Valves, Tubing
- Device/Instrument Housings
- Airway Management Devices: Endotracheal & Tracheotomy Tubes
- Laparoscopic Instruments
- Wound Dressings
- Class I, II, and III Medical Devices that come in contact with patients or their caregivers
- And many other applications

Design Considerations for Use of Antimicrobial Polymers in Medical Devices

For best results (efficacy, costs, etc.) and to speed up their development stage, medical device manufacturers are urged to be very specific in their initial design parameters so as to aid in the successful selection of antimicrobial materials and their dosage levels:

1) End-Use Environment
   Is the device in a dry or wet environment?

2) Product Life
   How long will the device be used? 24 hours? Three days? Three weeks? Duration of use can impact the biocompatibility, and antimicrobial efficacy can change with time in use.

3) Appearance
   Is a certain color required? Transparency? Translucency?

4) Preferred Base Polymer
   Antimicrobial compounds and their dosages can impact the processing parameters for polymers (e.g., high temperature limits).
Antimicrobial Coatings vs. Homogenous Antimicrobial Materials

While antimicrobial coatings can frequently avoid the processing challenges created by antimicrobial additives, the coating approach comes with its own limitations:

- Antimicrobial coatings are limited in efficacy to the surface, whereas materials with homogenous antimicrobial additives offer performance throughout the components for which they are used.
- Materials impregnated with antimicrobial properties maintain their efficacy when damaged or abraded.
- The uniformity of antimicrobial coatings must be closely monitored during a secondary, and often costly, manufacturing process, while using homogenous antimicrobial materials allows components to be effective right out of the mold.

Parker Antimicrobial Medical Device Components

With its decades of experience in elastomer formulation and processing, Parker Hannifin Corporation (a global leader in motion and fluid control technologies) is uniquely qualified to address the challenges created in adding antimicrobial properties to medical elastomers.

In particular, Parker has overcome many of the polymer processing limitations that have traditionally plagued antimicrobial compounds.

Parker’s antimicrobial/polymer combinations retain much, if not all, of their mechanical properties when compared to non-antimicrobial materials, and Parker’s medical elastomers have demonstrated both biocompatibility and 4+ log antimicrobial efficacy.

Parker Antimicrobial Elastomers for Medical Devices

- Butyl Rubber (IIR)
- Ethylene Propylene Diene Monomer (EPDM)
- Polyisoprene (IR)
- Polyurethane (TPU)
- Silicones (LSR and HCR)

Materials impregnated with antimicrobial properties maintain their efficacy when damaged or abraded.

The uniformity of antimicrobial coatings must be closely monitored during a secondary, and often costly, manufacturing process, while using homogenous antimicrobial materials allows components to be effective right out of the mold.
Silver- and Non-Silver-Based Antimicrobial Additives

Parker has tested a variety of antimicrobial compounds, both silver- and non-silver-based, in many of the most commonly used medical elastomers. Silver-based antimicrobial additives have the well-known benefits of efficacy, biocompatibility and wide medical industry acceptance; their disadvantages can include higher cost and discoloration. Non-silver-based antimicrobial additives can have similar efficacy and biocompatibility, little or no discoloration and more affordable costs; their main disadvantage is a less-developed medical history.

Antimicrobial Efficacy per ISO 22196

Parker’s medical molded polymers have achieved 4-log (99.99%) reductions in microbial count when tested to ISO 22196 standard; see Table 1.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Additive Type</th>
<th>Microorganisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid Silicone Rubber (LSR)</td>
<td>Non-Silver Silver</td>
<td>**</td>
</tr>
<tr>
<td>Silicone Rubber (HCR)</td>
<td>Non-Silver Silver</td>
<td>**</td>
</tr>
<tr>
<td>Polyurethane (TPU)</td>
<td>Non-Silver Silver</td>
<td>**</td>
</tr>
<tr>
<td>Butyl Rubber (IR)</td>
<td>Non-Silver Silver</td>
<td>**</td>
</tr>
<tr>
<td>Polyisoprene (IR)</td>
<td>Non-Silver Silver</td>
<td>**</td>
</tr>
</tbody>
</table>

Sterilization, Mechanical and Physical Tests of Antimicrobial Polymers

Sterilization Tests
Parker’s antimicrobial elastomeric compounds maintained a 4+ log reduction in bacterial activity compared to controls after steam, gamma, and EtO sterilization, as shown on Table 1.

Mechanical and Physical Tests
ASTM standard physical tests were run for tensile strength, tear strength, elongation, hardness, compression set and discoloration. Overall, Parker antimicrobial compounds largely maintain the mechanical properties of corresponding non-antimicrobial versions.
Biocompatibility per ISO 10993

Table 2 lists ISO 10993’s various device categories, contact conditions, contact durations and biologic effects. Because different material/antimicrobial combinations have differing performances and limitations, the medical device designer needs to carefully and fully describe the device’s application.

Many of Parker’s antimicrobial compounds, both silver-based and non-silver-based, have shown biocompatibility under various circumstances. Parker can review your needs and recommend the most appropriate solution.

Table 2: ISO 10993 Biocompatibility


<table>
<thead>
<tr>
<th>Device categorization by</th>
<th>Biologic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nature of body contact (see 5.2)</td>
<td>Contact duration (see 5.3)</td>
</tr>
<tr>
<td>Category</td>
<td>Contact</td>
</tr>
<tr>
<td>-----------</td>
<td>----------</td>
</tr>
<tr>
<td>Surface device</td>
<td></td>
</tr>
<tr>
<td>Intact skin</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>Mucosal membrane</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>Breached or compromised surface</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>External communicating device</td>
<td></td>
</tr>
<tr>
<td>Blood path, indirect</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>Tissue/bone/dentin+</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>Circulating blood</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>Implant device</td>
<td></td>
</tr>
<tr>
<td>Tissue/bone</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
<tr>
<td>Blood</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>X</td>
</tr>
<tr>
<td>C</td>
<td>X</td>
</tr>
</tbody>
</table>

X = ISO Evaluation Tests for Consideration  O = These additional evaluation tests should be addressed in the submission, either by inclusion of the testing or a rationale for its omission.

Note  + Tissue includes tissue fluids and subcutaneous spaces
Note ^ For all devices used in extracorporeal circuits
Why Parker?

Parker stands ready today to deliver elastomers that meet the challenges of hospital-acquired infections.

Parker’s Medical Systems Division, an integral part of Parker’s Engineered Materials Group, can jump-start your HAI-resistant device development process.

**High Performance Antimicrobial Elastomeric Compounds**

- Retain virtually all of the mechanical/physical strengths of conventional (non-antimicrobial) materials.

**Reduced Time-To-Market**

- Start your device design process with polymers that have proven ISO 22196 antimicrobial efficacy and ISO 10993 biocompatibility.
- Delegate the esoteric processing of antimicrobial materials to a Fortune 500 resource with decades of material engineering expertise for critical applications.
- Receive finished components from an ISO 13485 certified production facility, ready for integration into your medical devices.

**Custom Solutions Based On Your Specific Medical Applications**

- Allow our scientists and polymer engineers to aid you in the selection of antimicrobial additives and dosages based on your preferences for base polymers, aesthetics, and functionality for your specific device applications.
- Leverage our Finite Element Analysis (FEA) expertise to provide an accurate visualization of application performance and virtual prototype evaluation, while reducing the overall costs of program development.
- Utilize our injection molding simulation capabilities for thermoplastic materials to predict costly issues before they occur.

More Information

For additional details on Parker’s current range of antimicrobial polymers, contact:

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Citations

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