

Antimicrobial Efficacy

A Validated *In Vivo* Model for Device Implants

WuXi AppTec has developed an FDA-accepted animal model to test the efficacy of various antimicrobial agents when combined with devices. As post-implant device/site infections are a significant clinical issue, this model provides an infectious-agent-challenge methodology to evaluate antimicrobial therapeutics-device combinations.

[See reverse for an abstract on a study conducted using this model.]

WuXi AppTec is a global leader in providing discovery, testing and manufacturing services for the pharmaceutical, biotechnology and medical device industries. Research-driven and customer-focused, with operations in China and the U.S., WuXi AppTec offers a broad and integrated portfolio of services designed to assist our customers with cost-effective and efficient outsourcing solutions.

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Markets Served

- **Cardiology**
Antimicrobial devices coating and shell
- **Neurology**
Antimicrobial device shell
- **General Surgery**
Antimicrobial polymer mesh
- **Cranial Surgery**
Antimicrobial embedded in hydrogel
- **Orthopedic**
Polymeric drug delivery of an antimicrobial agent

Bacterial Strains

- Seven (7) clinically relevant bacterial strains are validated and available:
- Staphylococcus aureus
 - Staphylococcus epidermidis
 - Staphylococcus capitis
 - Escherichia coli
 - Acinetobacter baumannii
 - Pseudomonas aeruginosa
 - Methicillin-resistant Staph A (MRSA)

Species

- **Rabbit Model**
Validated (including regulatory review) and FDA accepted.
- **Alternative Methods**
Include mice, rats, dogs and pigs.

Model Steps

- **Surgery**
Device is implanted utilizing an aseptic surgical technique.
- **Inoculation**
Implanted device is inoculated with the appropriate strain.
- **Recovery**
After appropriate in-life period, the specific inoculated organism is recovered, including biofilm disruption, without non-specific contamination.
- **Sampling**
Multiple quantitative sampling techniques allow for quantitation of log reduction.
- **Terminal Analysis**
Consisting of bacterial quantification, efficacy analysis, biofilm examination and pathologic analysis.

Additional Analysis

- **Identification**
Identifies organism by DNA identification.
- **Zone of Inhibition**
Tests antimicrobial sensitivity to various bacterial strains.
- **Minimum Inhibitory Concentration (MIC)**
Quantifies antimicrobial concentration.

WuXi AppTec also performs other custom, preclinical implant studies, as well as complete biocompatibility/safety and toxicology testing.

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In Vivo Model of Human Pathogen Infection and Demonstration of Efficacy by an Antimicrobial Pouch for Pacing Devices

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ABSTRACT

Background: Device-related infections represent a significant clinical challenge. Once established, these infections prove difficult to treat with existing antibiotic regimens, compromising the health of device recipients, and usually requiring surgical intervention to resolve.

Objective: The purpose of this study was to determine the efficacy of the AIGIS_{RX}TM Anti-Bacterial envelope designed to reduce device-related infections by incorporating minocycline and rifampin in a controlled release polymer.

Methods: An infection was established in a rabbit model by creating bilateral subcutaneous implant pockets, into which a pacing device with or without AIGIS_{RX}TM was placed. The incisions were closed, and a defined dose of bacteria was infused into each implant pocket. After seven days, devices were explanted and sampled for viable bacteria by swabbing and sonication.

Results: Initial studies evaluated the ability of the AIGIS_{RX} pouch to reduce *Staphylococcus epidermidis* infection in this model using clinical and quantitative microbial endpoints. Results demonstrate *Staphylococcus epidermidis* infection in all control samples, while no pathogens were recovered from samples with the AIGIS_{RX}TM pouch. Systemic antibiotic levels were undetectable. Additional studies tested the efficacy of the AIGIS_{RX}TM pouch with additional bacterial strains, *Staphylococcus capitis*, *Escherichia coli*, and *Acinetobacter Baumannii*. In each case the device and implant pocket with the AIGIS_{RX}TM pouch was free of any signs of infection. An assessment of biofilm produced by *Acinetobacter* demonstrated the elimination of biofilm formation on the implanted device.

Conclusion: These results demonstrate that in this animal model, the AIGIS_{RX}TM device reduces the risk for infection of viable pathogens within implant pockets.

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