

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.]

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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 epidermis
 - 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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Development of Validated In Vivo Assays to Determine the Efficacy of Antimicrobial Products to Reduce Device-Related Infections

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Device-related infections represent a significant clinical problem, and remain the most common serious complication of medical devices. Once established, these infections prove difficult to treat with existing antibiotic regimens. Several new products are being developed aimed at incorporating antimicrobial drugs as a component of the implanted device itself to provide infection control at the site immediately upon implant. The demonstration of antimicrobial product efficacy requires animal models of implant infections in which a consistent, but non-lethal, implant infection is established. In response to the need to test the efficacy of several such anti-microbial products under development by several companies, WuXi AppTec (formerly AppTec Laboratory Services), a global contract testing company, has developed several animal models of device-related infections to test a wide array of products using several clinically relevant bacterial strains. This presentation will provide a review and discussion of such efficacy models. Because device-related infections can occur within a variety of implant sites, animal models of several different implant locations have been developed. Such implant sites include subcutaneous device implants, cranial implants to test dural sealant products, bone defects to establish osteomyelitis, and intraperitoneal implants. The established infections we have developed in these models include clinically relevant strains such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus capitis*, *Escherchia coli*, and *Acinetobacter baumannii*. A comparison of results using different bacterial strains, different implant sites, and different test article compositions indicate great variation in the dosing required to establish consistent infections under these different conditions. We have found that the development and severity of infection are dependent on different device geometries or surface characteristics. In studies in which an infection is established in a device-implant pocket, a biofilm is effectively created on the implanted device, as observed by scanning electron microscopy (SEM). Methods have been established to recover and quantify viable bacteria from the biofilm on the device, as well as from within the device pocket. The use of antimicrobial coatings or covers around the implanted device can completely inhibit the formation of such a biofilm and eliminate any detectable, viable bacteria from the inoculated pocket, as demonstrated in each of these infection models. In summary, the establishment of multiple animal models of device-related infections allows efficacy testing of a variety of antimicrobial products. In addition, a review of these studies provides insight into conditions necessary for the development of device-related infections.

**Presenting author*

Dr. Linda Hansen obtained her Ph.D. in Pathobiology from the University of Minnesota and post-doctoral fellowship in tissue engineering and cell biology at Harvard Medical School. She served on University of Minnesota faculty for several years before joining WuXi AppTec, Inc., in 2005, where she is Director of Custom Studies.



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