

## Novel BIOGUARD™ Antimicrobial Wound Dressing with Advanced NIMBUS<sup>®</sup> Technology

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## Abstract

FDA has cleared the novel BIOGUARD™ antimicrobial dressing featuring a permanently bound microbicide that provides long lasting microbial suppression in the dressing, generating an effective barrier to the transmission of pathogens. This technology assures the safest possible wound bed environment, and incorporates several features to prevent bacteria from becoming resistant. BIOGUARD dressings have been shown to be effective against common wound pathogens

and demonstrate the highest possible level of biosafety, by standard ISO biosafety tests, and by rigorous testing in mammalian cell models. This novel combination of efficacy, biocompatibility and safety, relative to bacterial resistance, offers a new cost-effective choice for caregivers to provide their patients with a barrier dressing suitable for prophylactic measures against nosocomial infections.

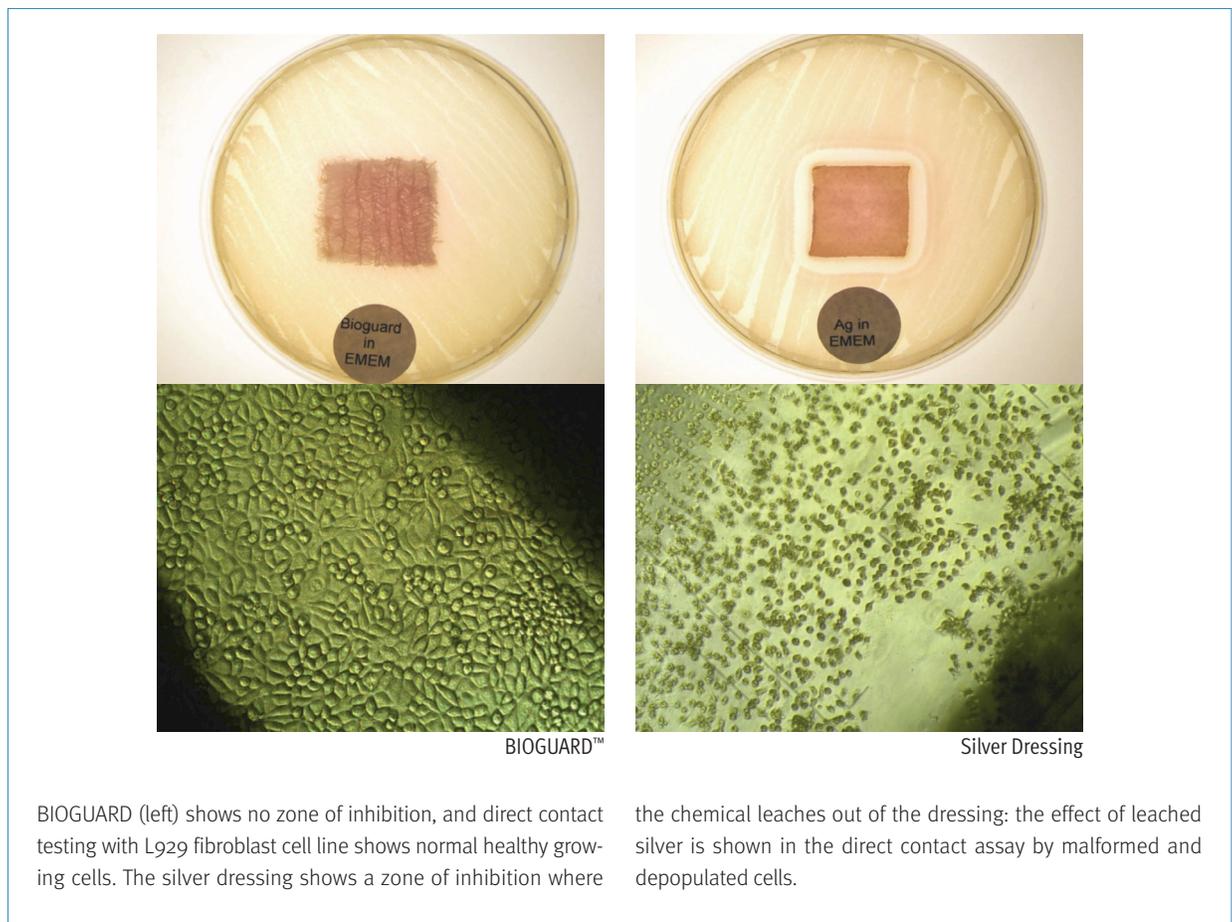
## Background

The dangers of bacterial colonization in wounds are well understood by caregivers—particularly because compromised surfaces are the primary point of vulnerability for the patient. BIOGUARD antimicrobial barrier dressings optimize efficacy and safety to provide caregivers the ability to safely apply the dressings prophylactically to help prevent pathogen transfer. Other currently available antimicrobial dressings act by leaching antimicrobial agents into the wound bed (see section on Zone of Inhibition and Figure 1). This approach is successful in reducing wound colonization, but released small antimicrobial

molecules may select for bacterial resistance, cause skin discoloration/ reaction, or impede wound healing (Wang et al, 2009; Silver et al, 2003; Van Den Plas et al., 2008).

Additionally, the cost of many current antimicrobial dressings keeps them out of reach of many patient populations for regular use. BIOGUARD dressings were designed to provide an antimicrobial barrier technology that is effective, economical, and safe enough for broad application.

**Figure 1: Zone of inhibition plates (*E. coli*) and direct contact cytotoxicity tests for BIOGUARD and for a silver dressing.**



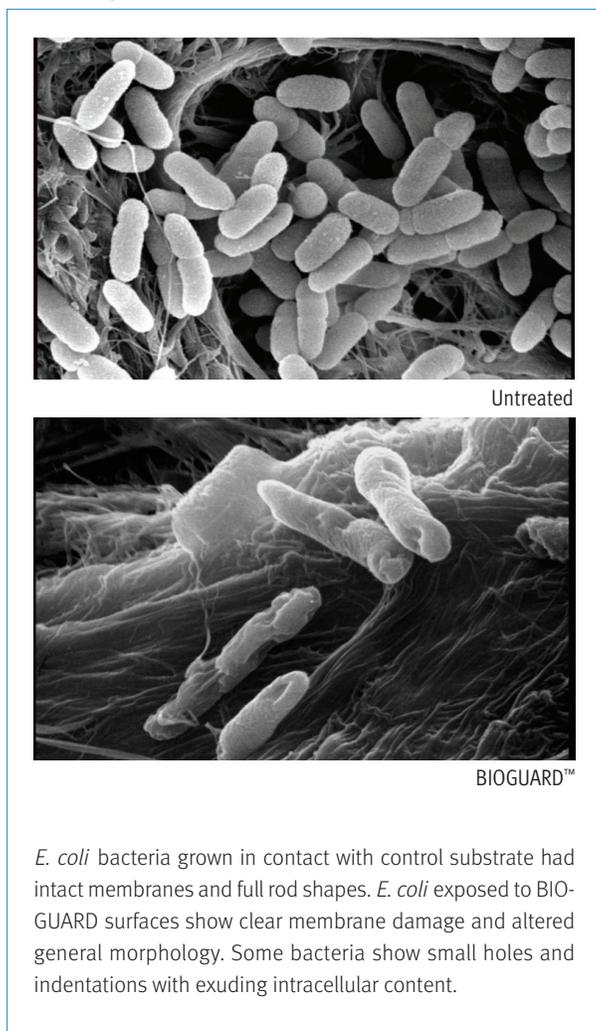
BIOGUARD (left) shows no zone of inhibition, and direct contact testing with L929 fibroblast cell line shows normal healthy growing cells. The silver dressing shows a zone of inhibition where

the chemical leaches out of the dressing: the effect of leached silver is shown in the direct contact assay by malformed and depopulated cells.

## Mechanism of Antimicrobial Activity

The BIOGUARD antimicrobial barrier dressing is based on the patented NIMBUS® technology (Quick-Med Technologies, Inc.). The active antimicrobial agent is permanently bound to the dressing surface, and acts on the wound pathogen by physically disrupting the prokaryotic cell wall. Electron micrographs (Figure 2) show *Escherichia coli* cells before and after contact with BIOGUARD. The top panel shows healthy intact cells, while the bottom panel shows disrupted and lysed cells—deflated membrane sacs with their intracellular contents released. This process does not rely on the agent entering the cell: the physical size of the polymeric antimicrobial precludes entry into the cell, even if the polymer were not permanently bound to a solid surface. Lysis of the cells is induced from outside, preventing bacterial cells from being able to generate resistance to the antimicrobial polymer, as all known acquired resistance mechanisms are cellular adaptations to small internalized agents—either through efflux mechanisms or re-routing of metabolic pathways (Poole, 2002).

**Figure 2: Scanning Electron Microscope images of *E. coli* on untreated gauze and on BIOGUARD.**



The macromolecular agent responsible for BIOGUARD’s mode of action is poly(diallyldimethylammonium chloride), or polyDADMAC, a cationic quaternary ammonium polymer. Polycationic agents combine broad-spectrum antibacterial activity with relatively low toxicity, allowing use in contact lens cleaning solutions (Hibbard, 2005), topical antimicrobial preparations (Kramer et al, 2004; Daeschlein et al, 2007) and in wound dressings (Lee et al, 2004). The most similar molecule currently used in wound dressings is PHMB (Poly-HexaMethylene Biguanide); the main important difference being that the polyDADMAC molecule is approximately 100 times larger. Literature reports that molecular size is important because the level of toxicity to eukaryotic cells induced by cationic biocides is inversely related to the size of the molecular chain (Ikeda, 1991; Gilbert and Moore, 2005).

### Antimicrobial Testing

Wound pathogen	ATCC #	Average kill
<i>Staphylococcus aureus</i>	ATCC 6538	99.999992%
MRSA	ATCC BAA-44	99.999998%
<i>Staphylococcus epidermidis</i>	ATCC 12228	99.999997%
<i>Pseudomonas aeruginosa</i>	ATCC 15442	99.99999%
<i>Enterococcus faecium</i>	ATCC 19434	99.999987%
<i>Escherichia coli</i>	ATCC 8739	99.999997%
<i>Acinetobacter baumannii</i>	ATCC 19606	99.999999%
VRE	ATCC51299	99.999991%

### Zone of Inhibition

The BIOGUARD dressing is different from other antimicrobial dressings in that it does not have a zone of inhibition (Figure 1). The bound antimicrobial protects the dressing without leaching any chemical agents, and therefore nothing cytotoxic that could retard healing enters the wound bed. Also, the absence of a leached agent ensures the absolute minimum possibility for bacteria to develop resistant strains.

**Testing Summary**

Test Type	Test Method	Result for BIOGUARD
Antimicrobial Efficacy	“Antibacterial Finishes on Textile Materials, Assessment of” (AATCC method 100-1998)	Strong antimicrobial efficacy: >99.9999% for common wound pathogens
Cytotoxicity	Agar Diffusion Overlay Method (ASTM F895-84)	Lowest cytotoxicity score possible. Non-cytotoxic per test evaluation
	Direct Contact Method with L929 cell line (ASTM F813-07)	Non-cytotoxic per test evaluation
Dermal Irritation	Primary Skin Irritation (ISO 10993-10 guidelines)	Lowest irritation score possible in test: evaluated as negligible irritant
Dermal Sensitization	Repeated Patch Dermal Sensitization (Buehler Method)	Lowest sensitization score possible in test: no sensitization observed
Zone of Inhibition	Inhibition test on <i>E. coli</i> plate	No growth on or under dressing; no visible inhibition away from dressing surface
Bacterial Resistance	Antimicrobial efficacy of step-wise adapted survivor cultures	No change in antimicrobial efficacy of the BIOGUARD dressing for 10 iterations of step-wise adapted cultures
	MIC of step-wise adapted survivor cultures	No change in MIC of BIOGUARD active for <i>E. coli</i> over 10 iterations of step-wise adapted cultures

**Safety and Biocompatibility**

BIOGUARD dressings were exhaustively tested for safety and biocompatibility. Direct dermal testing included skin irritation and sensitization, showing no irritation or sensitization. Sensitive *in vitro* models were used to assess cytotoxicity by multiple methods, including not only agar diffusion but also direct contact testing on fibroblast cell lines. This demonstrates that BIOGUARD impeded cellular growth no more than negative controls, while a silver dressing showed significant cytotoxicity in the same assay. Testing of step-wise adaption for 10 iterations showed that bacteria did not develop resistance to the BIOGUARD dressing.

**Conclusions**

The BIOGUARD dressing demonstrated high efficacy against common wound pathogens, while maintaining the highest possible level of biosafety. This is most clearly illustrated by Zone of Inhibition testing: the lack of an inhibitory zone confirms that BIOGUARD antimicrobial barrier dressing is able to control pathogens in the dressing without exerting a physiological effect on the wound bed. A silver dressing tested alongside showed a zone of inhibition, and showed retardation of cells in mammalian cell models. Since the BIOGUARD antimicrobial barrier dressing is shown to be able to fulfill its protective function without impeding cells relevant to wound healing, and without causing concern over bacterial resistance, it is safe enough to be used broadly as a prophylactic device to protect vulnerable patients and wounds from infection without adding risks for the patient.

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