BIOGUARD™ Barrier Dressings: No Bacterial Resistance Issues

BARRIER DRESSING BIOGUARD™

Advanced NIMBUS® Technology Provides Unparalleled Safety

BIOGUARD™ dressings with advanced NIMBUS® technology represent the next generation in antimicrobial wound care. They employ a very large polycationic polymer molecule, which is permanently bound to the substrate material of the wound dressing. The NIMBUS antimicrobial agent, poly(diallyldimethylammonium chloride) or pDADMAC, is a polyquaternary ammonium compound (polyquat) similar to smaller agents such as benzalkonium chloride, chlorhexidine and PHMB, but with the important distinction that it is hundreds of times larger.

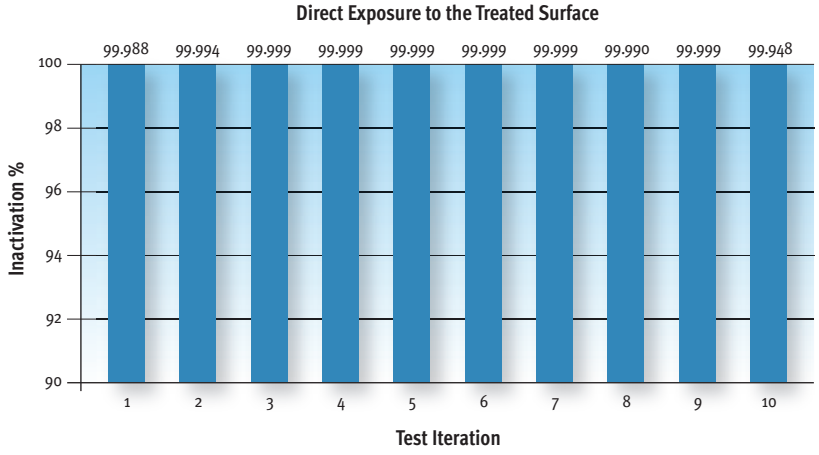
Unique Technology—Large Molecule, Permanently Bound

The unique aspect of BIOGUARD's NIMBUS technology is that the very large pDADMAC molecule is permanently bound to a surface, so it cannot migrate into a wound and kill wound cells (fibroblasts, epithelial cells, vascular endothelial cells) or become depleted with use.

This is in contrast to small molecule antimicrobials utilized in wound care, such as silver or small quats, where the agent leaches out of a dressing and into the wound bed. The very large size of the pDADMAC molecule makes it very effective at disrupting bacterial cell membranes and makes it nearly impossible for bacteria to evolve a defensive mechanism.

No Bacterial Resistance Developed

NIMBUS antimicrobial technology was evaluated to determine the degree of susceptibility of resistance to the agent. The Gram-negative bacteria, *Escherichia coli*, was selected because its cell wall construction is very hardy and has relatively low susceptibility to quaternary ammonium agents. *E. coli* were exposed to NIMBUS on the BIOGUARD surface, and survivors were isolated, cultured and re-exposed for ten successive experiments in which bacteria multiplied a million-fold during each experiment. NIMBUS killing efficacy remained constant through-out ten iterations, showing that the bacteria had not increased resistance to pDADMAC.



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No Bacterial Resistance

NIMBUS dressings possess several qualities that make generation of resistant bacteria highly improbable. The pDADMAC polymer is extremely large and highly charged. The high charge density quickly destroys bacterial cell walls by displacing the calcium cation that stabilizes the structure of the cell walls, leading to holes in cell membranes and eventual collapse and death of the bacteria. The molecule is also physically far too large to enter a cell, even if it were not permanently bound to a surface. The permanent bond ensures that the concentration of the antimicrobial agent (as gauged by charge density) remains above the Minimum Inhibitory Concentration on the surface, but without any low-concentration zone away from the surface of the dressing.

High Charge Density

The high positive charge or charge density of a polyquat is based on molecular size. BZK has a molecular weight of 354 and has one cationic site. CHG has a molecular weight of 898 and has two cationic sites. The number of cationic sites per molecule of pDADMAC, which has a molecular weight of 200,000 to 250,000, is over 1,500.

Molecule	Type of Molecule	Molecular Weight, g/mol
Penicillin	Antibiotic	373
Ciprofloxacin	Antibiotic	386
Vitamin B12	Vitamin	1355
Benzalkonium chloride	Cationic microbicide	354
Chlorhexidine gluconate	Cationic microbicide	898
PHMB	Polycationic microbicide	~2,000-4,000
Poly-DADMAC	Polycationic microbicide	~200,000-250,000

No "Low Dosing" Issues

Adaptation is a response that bacteria can have when exposed to low doses of antimicrobial agents. The Minimum Inhibitory Concentration (MIC) of an antimicrobial refers to the lowest concentration that will still inhibit the growth of bacteria. When exposed to antimicrobial concentrations below MIC there are surviving bacteria that have a slightly higher tolerance for an agent. Over the course of generations of bacteria, continual selection for the bacteria most tolerant of exposure to antimicrobial agents at low concentrations yields a more resistant population. This effect will occur for antibiotics as well as non-bound antiseptics, because these small agents readily diffuse to create a concentration gradient at some distance from the source. NIMBUS avoids a concentration gradient by permanently binding the antimicrobial agent to a surface.

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Bacterial Resistance: An Important Consideration in Selecting Antimicrobial Dressings

Antimicrobials commonly used in dressings can cause bacteria to develop resistance. Silver, PHMB and triclosan are capable of selecting for or causing bacterial resistance.[1, 2, 3, 4, 5]

The mechanism by which antimicrobials destroy bacterial cells varies with the chemistry of the agent. It is especially important for applications such as medical devices to choose an antimicrobial chemistry that is unlikely to generate bacterial resistance.

[1] Gupta, A., et al, *Nature Medicine* **5**: 183-188. (1999)
[2] Moore, L.E., et al, *Appl. Environ. Microbiol.* **74**: 4825-4834 (2008)
[3] Allen, M.J., et al, *Microbiology* **152**: 989-1000 (2006)
[4] Mclvlurray L.M., et al, *Nature* **398**: 531-532 (1998)
[5] Heath, R. J., et al, *J. Biol. Chern.* **273**: 30316-30320 (1998)

"NIMBUS poses no danger of bacteria developing resistance, or of releasing toxic material into the wound and impeding the healing process. It is a novel technology: bonded and effective even in high concentrations of body fluids."

— Gregory Schultz, Ph.D.
Professor, Institute for Wound Research, University of Florida
Past President,
Wound Healing Society