**Testing leading to a "de novo" (i.e., no predicate) FDA cleared antimicrobial wound dressing**

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**Statement of Purpose:** Based on the expressed need for an antimicrobial dressing by a surgeon, a variety of treatments for gauze were developed and tested. After finding a poly quaternary ammonium polymer that gave results much better than expected (no inhibition of activity in serum), an attempt was made to obtain clearance by the FDA. However, it was found that the predicate devices chosen, such as silver-based advanced wound dressings, did not in fact reflect the behavior of the new device submitted. Hence, a de novo route was required for clearance instead of the traditional 510(k) clearance. This involved extensive testing, and development of new tests to demonstrate safety and efficacy. Those tests and the results leading to eventual clearance and commercialization are described in this presentation as well as the synthesis methods to create this novel surface modification. Some results of use in a burn clinic will also be described. (ref 1).

**Methods:** (materials and analytical procedures used) Ordinary medical gauze was used as a substrate for surface treatments. First experiments followed traditional methods based on creating free radicals on the surface via oxidation and then polymerizing monomers that had appropriate functional groups: quaternary ammonium groups. However, this produced relatively low molecular weight chains that had interesting activity against bacteria, but the surfaces could be inactivated by exposure to serum in some cases, and the chemistry was expensive. One monomer, diallyl-dimethyl-ammonium chloride (DADMAC) was most promising, and variations of attaching that polymer were tried. Subsequent optimization of this method led to higher molecular weight polymers attached to the surface, and more successful killing of microorganisms. (ref. 2). However, the most successful methods involved using the preformed polymer in a wash solution that was immobilized by a heat treatment of the gauze and subsequent washing (ref 3). The amount of retained pDADMAC could be followed with adsorption of anionic dyes to the gauze. A variety of testing methods were tried, and some new ones developed, for efficacy. A significant amount of new testing was required for the FDA de novo process since there were no predicates on the market. For instance, no zone of inhibition was measurable for the the new dressings.

**Results: The antimicrobial efficacy of BIOGUARD dressings on various wound pathogens was outstanding using a modified ATCC method 100 protocol ; (all >99.9999% kill):** *Escherichia coli* ATCC 15597 *Staphylococcus aureus* ATCC 6538 MRSA (Methicillin resistant *S. aureus*) ATCC BAA-44 *Staphylococcus epidermis* ATCC 12228; *Pseudomonas aeruginosa* ATCC 15442; *Enterococcus faecium* ATCC 19434; VRE (Vancomycin resistant *Enterococcus faecium*) ATCC 51299

Exposure of the dressings to human fibroblasts showed minimal toxicity in comparison to the highly toxic effect on bacteria. Other experiments suggested no development of antibiotic resistance. These results, and the FDA clearance, led to licensing to Dermasciences, Inc. which introduced the gauze dressings as BIOGUARD. A brief summary of some barrier properties was published (ref. 4), but details of the synthesis and testing will be presented here.

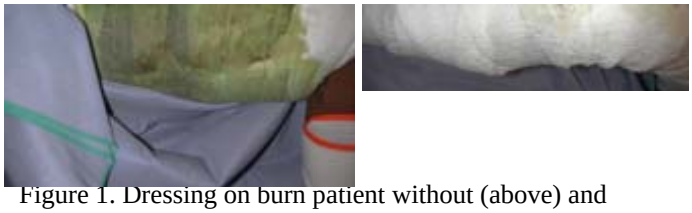

Figure 1. Dressing on burn patient without (above) and with (below) new dressing. (ref. 1)

**Conclusions:** A novel microbicidal wound dressing with a bound microbicidal "polyquat" polymer was cleared by the FDA using the "de novo" pathway rather than the more typical "510k". Initial clinical assessments demonstrated dramatically reduced levels of bacterial growth in the BIOGUARD dressing in heavily exudative wounds. Additional clinical studies will assess the level of aerosolization of bacteria during dressing changes and risk of wound infection.

**References:**

1. 2011, Youngblood et al., Symposium on Advances in Wound Care: Gauze Bandages with a Bound Antimicrobial Substrate Suppress Bacterial Growth in Patients with Heavily Exudating Wounds (poster)

2. USPatent #7,709,694, "Materials with covalently-bonded, nonleachable, polymeric antimicrobial surfaces"; Batich; C, Schultz; G.; Mast; B.; Olderman; G.; Lerner; D.; Toreki; W. (issued May 4, 2010).

3. USPatent # 7,790,217 Toreki; William ; "Method of attaching a bound microbicide to a device" Liesenfeld; Bernd; Moore; David; Leander, Susan; Batich; Christopher (issued September 7, 2010)

4. Albina Mikhaylova, Bernd Liesenfeld, David Moore, BS;1William Toreki, Jillian Vella, Christopher Batich, Gregory Schultz, "Preclinical Evaluation of Antimicrobial Efficacy and Biocompatibility of a Novel Bacterial Barrier Dressing" WOUNDS 2011;23(2):24–31