

Presented at Meeting of the FDA's General and Plastic  
Surgery Devices Advisory Panel  
September 20-21, 2016

## Trial Design, Endpoints, and Resistance

Marissa J. Carter, PhD, MA, MAPWCA  
President  
Strategic Solutions, Inc.



**Strategic Solutions, Inc.**

# Points to Consider

- Complete wound healing as an endpoint is inappropriate
- Current claims are based on containing infection (antimicrobial barrier) while dressing absorbs exudate
- Classic infection endpoints and in-vitro data may be helpful to support existing claims
- Some currently used secondary endpoints support real world use of antimicrobial dressings
- new treatments for topical antimicrobial products might justify device risk reassessment; PMA as approval route.
- Unlike antibiotics, no evidence that resistance is a problem with antimicrobial dressings in wound care.

Dr Carter is a clinical trial designer/manager, epidemiologist, biostatistician, health economist, and EBM practitioner; she has published over 100 articles in these fields.

# Antimicrobial Dressing Trials: Wound Healing

- Efficacy for antimicrobial dressings in controlled trials or effectiveness in “real world” studies is **NOT** about wound healing
- The main goals or even claims for antimicrobial dressings have nothing to do with complete wound healing
- Most trials to date were not large enough to properly analyze complete wound healing anyway
- This is why the majority of systematic reviews did not find evidence for wound healing.

# Topical Antimicrobial Product Trials

- Some currently used endpoints are not practical because of the situation with multiple interventions driven by changing wound needs
- Classic infection endpoints such as quantitative bacterial counts have been used but only make sense when systemic antibiotics are not used (confounding issues)
- Most controlled trials carried out to date have included safety endpoints based on adverse events but these may not help in understanding resistance
- Many controlled trials had secondary endpoints, such as odor, exudate management, and pain reduction
- These are the targets not only for controlled trials but very useful in the **real world**.

# Silver-Impregnated Dressings: RCTs, Secondary Endpoints

SS: statistically significant

Study	Use (days)	# Dressing Changes	Epithelialization increase	Odor	Exudate Management	Pain reduction
Dimakakos**	63	18				SS
Jorgensen	28	6		SS	SS	
Jude	56	>=8				
Jurczak	14	Ave 11			SS	SS
Lazareth	28	Unknown				
Meaume	14	10				
Munter	28	10-15 exudate	SS	SS	SS	SS
Wunderlich & Orfanos	42	Unknown	SS			

# Claims

- Current claims are based on preventing spread of infection or being an effective antimicrobial barrier while the dressing absorbs exudate
- Different claims would require new endpoints.

# Recommendation for Device Classification

- Recommendation: Antimicrobial dressings should be regulated as **Class II Medical Devices under the 510(k) Premarket Notification process.**
- The evidence coming from studies employing antimicrobial dressings indicates that the risks of providing barrier technology to support bioburden control are understood and very low
- If different claims are needed for new products, different endpoints might be needed, or a PMA might be appropriate when a new product has novel mechanisms of action

# Resistance to Antimicrobial Agents

- Unlike antibiotics, these antimicrobial agents have multiple mechanisms of action, thus lowering risks of resistance
- Controlled trials not a good way to understand trends of resistance to antimicrobial agents.
- Resistance to local antimicrobial agents has been measured in some wound care studies and is **minimal or cannot be found**.

# Path Forward

- Current level of evidence suggests that probable benefits outweigh probable risks in the majority of the wound care population
- The resistance issue is bigger than just local antimicrobial agents as majority have **NOT** been associated with antibiotic-like resistance and on a mechanistic basis do not elicit that type of resistance
- **Misuse of antibiotics to treat wounds, which is often not effective, should be the real concern.**