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Trial Design, Endpoints, and Resistance

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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

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<th>Study</th>
<th>Use (days)</th>
<th># Dressing Changes</th>
<th>Epithelialization increase</th>
<th>Odor</th>
<th>Exudate Management</th>
<th>Pain reduction</th>
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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.