Title: Feasibility of Pre-operative Povidone Iodine Decolonization among Orthopedic Trauma Surgery Patients To Reduce *S. aureus* SSIs
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Background
Our previous multicenter study of a bundled intervention to prevent *S. aureus* surgical site infections (SSI) resulted in a 42% decrease in complex *S. aureus* SSIs (rate ratio = 0.58; 95% CI, 0.37 to 0.92) among hip, knee and cardiac surgery patients.[1] The evidence-based bundled intervention included screening for *S. aureus* nasal colonization, decolonizing carriers with intranasal mupirocin and chlorhexidine gluconate body wash, and prescribing optimal perioperative antibiotics. However, even among elective orthopedic procedures, compliance with this intervention was less than ideal.

Decolonization interventions such as this have not been rigorously investigated in trauma surgery populations, because of the expeditious and non-elective nature of trauma care. Pre-operative decolonization with mupirocin is impractical to complete in the vast majority of patients with orthopaedic trauma. Dr. Michael Willey, an orthopaedic trauma surgeon, went to great lengths to implement *S. aureus* screening and mupirocin decolonization of carriers among his patient population at University of Iowa Hospitals and Clinics (UIHC). Yet, even with full surgeon support, compliance with *S. aureus* nasal screening was 80% and compliance with mupirocin was only 41%. Thus, there is great interest in determining whether a simpler intervention using povidone-iodine (PROFEND®) nasal decolonization could be implemented into the clinical process of care and reduce rates of surgical site infections (SSI) in this very high-risk population.

PROFEND® nasal decolonization has the potential to be an efficient and low-cost intervention to reduce rates of SSI.[2,3] Although orthopaedic trauma patients are at high risk of SSI, our sample size and power calculations found that a study evaluating the effectiveness of nasal PROFEND® for reducing deep SSI in this population would need ~1,000 patients, and thus would require participation by multiple hospitals. A pilot study evaluating the feasibility of administering PROFEND® among patients undergoing orthopaedic trauma procedures could inform the development and implementation of a large, multicenter study.

This proposal describes a small, phase IV post-marketing study to assess the best way to implement this FDA approved product among surgical patients.

Study design
Implement PROFEND® pre-operative decolonization for individuals undergoing operative fixation of lower extremity fractures and evaluate the feasibility of this intervention.
Aim 1. Evaluate patients 24 hours after surgery to determine *S. aureus* colonization and to survey patients on tolerability of PROFEND® decolonization.

Patients will be tested for *S. aureus* nasal colonization prior to surgery, the evening after surgery and on the day after surgery. At each time point, a dry, sterile, rayon swab will be used to sample the anterior apex portion of the right and left nostril. The swab will be immersed in a tube of 1 mL neutralizing solution (75 mM phosphate buffer containing 1.0% lecithin, 0.1% Triton™ X-100, 5.0% polyoxyethylene sorbitan monooleate, and 0.5% sodium thiosulfate, pH 7.9 + 0.1) and capped tightly. The swabs will be inoculated into 1mL broth and vortexed for 15 seconds. Serial dilutions will be performed and plated on media. The cultures will be quantitatively assessed to determine the $\log_{10}$ reduction in *S. aureus* after use of PROFEND®. For semi-quantitative cultures the swabs will be inoculated into 5mL broth, incubated with agitation overnight for a broth enrichment step. After 24 hours, 10uL will be plated onto the first quadrant of the media and each successive quadrant will be streaked using a new bacteriologic loop in order to dilute the number of bacteria in each quadrant. The culture results will provide information we will need when designing a large multicenter study of PROFEND®. The

PROFEND® swab will be administered to the patient's nares following this initial sample around one hour prior to the first surgical incision. It will then be re-applied around 12 hours later, for a total of two applications within a 24 hour period.

During the same visit at 24 hours after surgery, patients will also be administered a questionnaire to determine the tolerability of PROFEND® decolonization. Questions will be asked about adverse events (e.g., itching, irritation) and how PROFEND® felt (very pleasant, pleasant, neutral, unpleasant, very unpleasant). The adverse event question will be the same as a question that we have already asked 183 patients who received mupirocin. Thus, we will be able to compare these results with one another.

Based on the data obtained from this aim, we will summarize the patient acceptance of PROFEND®.

References

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