Defining Processes to Manufacture Sterile Antiseptics
E. J. Elder 1, K. J. Jones 1, A. C. Schuelke 1, V. M. Echeverria 1, J. C. Walton 1, M. J. Sacchetti 1, P. K. Basu 2, D. Hussong 3
1 University of Wisconsin - Madison, 2 National Institute for Pharmaceutical Technology and Education, 3 U.S. Food and Drug Administration

Purpose
To assess the impact of various sterile manufacturing technologies on topical antiseptic products. These products are often used on skin to eliminate microorganisms prior to surgery and reduce the risk of infections. The common assumption is that these solutions kill microorganisms and manufacturing of the solutions does not require additional processing to render them sterile. However, recent product recalls resulting from microbial contamination have demonstrated that these products do support microbial growth. When this happens, the attempt to disinfect skin results in applying microbial contamination to the surgical site.

Methods
Analytical methods were validated for chlorhexidine gluconate (HPLC), benzalkonium chloride (HPLC), ethanol (GC), isopropanol (GC), and povidone-iodine (titration). Seventeen commercial products were purchased, tested, exposed to sterilization processes, and then re-tested. Sterilization processes included: standard autoclave (steam) cycle (121°C / 15 min), low temperature autoclave cycle (118°C / 25 min), standard ethylene oxide cycle (EtO), electron beam (15 kGy, E-beam), and filter compatibility testing.

Results
Steam sterilization destroyed package integrity for many products, even at low temperature cycle; however, most applicators were not affected by the processing conditions. E-beam and EtO maintained most package integrity; however, a noted potency reduction occurred in some E-beam samples and several alcohol samples had package integrity issues with EtO (dried out). Filter materials compatible with each liquid product were identified.

Conclusion
Sterilization techniques are available for processing topical antiseptic products. Implementation of sterilizing technologies may require multiple processing steps, additional specific equipment and/or aseptic processing for assembly and packaging of some products; however, this would mitigate the potential risk associated with microbial contamination of non-sterile topical antiseptic products.

This work was supported by FDA grant NIPTE-UO1-UW-002-2012 through the DHSS, PHS grant 5U01FD004275-02 to the National Institute for Pharmaceutical Technology and Education (NIPTE).