ALLIANCE OF
WOUND CARE
STAKEHOLDERS
POWER THROUGH COLLECTIVE ADVOCACY

September 1, 2016

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane Room 1061
Rockville, Maryland 20852

Submitted electronically to www.regulations.gov

Re: Docket Number FDA-2016-N-2147 General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee; Notice of Meeting: Establishment of a Public Docket; Request for Comments

Dear General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee;

On behalf of the Alliance of Wound Care Stakeholders ("Alliance"), we are pleased to submit the following comments in response to the September 20-21, 2016 Food and Drug Administration's meeting of the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee. The Alliance is a nonprofit multidisciplinary trade association of physician medical specialty societies, clinical and non-clinical associations, and business entities whose mission is to promote quality care and access to products and services for people with wounds through effective advocacy and educational outreach in the regulatory, legislative, and public arenas. These comments were written with the advice of our members who not only possess expert knowledge in complex chronic wounds, but also in wound care research. Since our healthcare provider members prescribe antimicrobial wound care products in their practices and our company member manufacture these products, we have a vested interest in this issue. A list of our members can be found at: www.woundcarestakeholders.org.

GENERAL COMMENTS

The Alliance members believe that the products that are currently in the FRO category are low to moderate risk, have been in the marketplace for many years, and should be classified by the FDA into either Class I or Class II, most remaining subject to 510(k). Members of the Alliance will be speaking at the upcoming public meeting, but we wanted to provide information to the Panel in advance to address many of the issues that validate our recommendation. Our comments will address:

- Overview of wound care relating to the FRO product category
- Science behind management of chronic wounds
- Management of chronic wounds using antimicrobial wound care products
- Products classified in the FRO product category, their indications for use and testing

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- Evidence for safety and effectiveness of products in FRO category/ Low-moderate risk of antimicrobial resistance
- Additional issues for FDA consideration

OVERVIEW OF WOUND CARE RELATING TO FRO PRODUCT CATEGORY

One can categorize wounds into three types relating to their causality: chronic, acute or burns. While the products that are included in the FRO category may be used for any of these types of wounds, our comments are related to management of chronic wounds, such as venous insufficiency ulcers, diabetic foot ulcers, pressure and arterial ulcers. Chronic ulcers are devastating clinically and have an extraordinary impact on patients. From a recent study we conducted, we found that chronic wounds impact nearly 20% of Medicare beneficiaries which translates into over 11 million people in that group alone. (in manuscript)

Some compelling information about wound care that we believe that the Panel should know:

- *There many different specialists who treat patients with chronic wounds whose contributions to care must be captured:* The practice of wound care is not limited to one particular medical specialty recognized by the American Board of Medical Specialties. Instead, many different specialists are involved in the management of patients with chronic wounds. These practitioners include but are not limited to the following: surgeons (e.g. vascular surgeons, plastic surgeons, and foot and ankle surgeons), vascular medicine physicians, podiatrists, dermatologists, nurse practitioners, infectious disease experts, physical therapists, nurses, registered dietician nutritionists, and primary care physicians who are in the full time practice of managing patients with wounds.

- *Wound care patients often have co-morbidities.* Non-healing wounds occur among patients with diabetes, peripheral vascular disease (nearly as common as coronary artery disease and stroke), or as a result of unique medical problems (e.g., sickle cell anemia, vasculitis), or in association with immunosuppression (e.g., AIDS, chemotherapy, steroid use or transplantation medications). Many times the wound care costs, human and financial, are not taken into account since these patients may enter the hospital with a primary diagnosis of infection, cardiac impairment, diabetes, kidney failure or cognitive deficits, and the diabetic foot ulcer or venous insufficiency ulcer may not be noted; therefore, contributing to an underreporting of wound care needs and resulting expenditures. Specifically, for patients with pressure ulcers, the most common primary diagnoses for hospitalizations include septicemia, pneumonia, urinary tract infections, congestive heart failure, respiratory failure, and complicated diabetes mellitus.[i]

- *Wound healing is a complicated process directly influenced by the status of the local wound environment as well as by the overall physical condition of the individual.* The process of wound healing involves metabolic, structural, biochemical and patient factors in a unique way. Wound healing is not a single event; it is a result of complex overlapping processes. There are guideline-suggested interventions, but there are many combinations of individual wound characteristics which contribute to the complexity of healing a wound. Chronic wounds are dynamic and the wound needs often change, requiring the order and combinations

of treatments to be varied based upon frequent wound assessments and may be used anywhere along the wound healing cascade. In other words, the chronic wound changes as it progresses and there are multiple modalities, procedures and products used to treat it at that same time and over its course of healing.

- *Chronic wounds may fail to heal, and even when they do, their recurrence rate approaches 80% because little can be done to mitigate the risk factors associated with their development.*[ii]

- *Treating patients with chronic wounds is complex.* We want FDA and the Panel to appreciate the complexity of taking care of patients who have chronic wounds. The following is an example of procedures and products associated with treating a patient with a diabetic foot ulcer. Many of these procedures are taken from the 2016 clinical practice guideline by the Society for Vascular Surgery created in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine.[iii] Using the wound care products that are regulated in the FRO category are only part of the care which may utilize multiple devices, drugs and interventions.

Comprehensive care associated with the treatment of a diabetic foot ulcer (DFU) could include the following:

- Outpatient office visits (wound care centers, physician offices, home care, and skilled nursing facilities)
- Hospitalizations for wound and non-wound related complications
- Prevention of diabetic foot ulceration (office visits)
    - Patients undergo annual interval foot inspection by physicians
    - Foot exams include testing for peripheral neuropathy using the Semmes-Weinstein test
    - Patient educated by physician and staff about preventive foot care
    - Use of therapeutic footwear
    - Adequate glycemic control
    - Arterial-brachial index (ABI) at age 50 or for any at-risk patient who is diabetic that presents with a new onset ulcer (includes patients on immunosuppressive therapy, steroids, or medical history preempts the need to perform an ABI)
- Development of foot ulcer (office visits)
    - Doctor accesses for ischemia, infection and neuropathy
    - Doctor offloads the foot
        - Plantar diabetic foot ulcer use total contact cast or irremovable fixed ankle walking boot
        - Non-plantar—use modality that relieves pressure at the site of the ulcer (heel relief shoe)
    - Doctor performs comprehensive wound care which may include the following procedures/modalities/products depending on how well the wound heals:
        - Sharp debridement/surgical intervention for callus and non-viable necrotic tissue, which involves removing bioburden and bacteria from the wound
        - Application of surgical dressings to maintain moist wound bed

    - Sharp debridement at 1-4 week intervals based on amount of callus and non-viable tissue that developed between visits
    - After 4 weeks if not improved, apply adjunctive wound therapy options: negative pressure wound therapy, cellular and/or tissue based products for skin wounds, hyperbaric oxygen therapy including reassessment of current wound etiology and treatment plan
    - If doctor suspects soft tissue abscess or osteomyelitis, then use MRI
        - If osteomyelitis is present, then bone debridement procedure, biopsy and culture, antibiotics and/or hyperbaric oxygen therapy
    - If doctor diagnoses clinically significant peripheral artery disease, then need to perform revascularization (either surgical bypass or endovascular therapy)
- Amputation, revision and reconstruction procedures (These would include hospitalizations, office visits as well costs associated with home health visits, physical therapy visits, prosthetist visits and prosthetics and orthotics used.)
- Management associated with durable medical equipment prescribed (e.g., off-loading devices, Charcot restraint orthotic walker [crow walker], wheelchairs.

SCIENCE BEHIND THE MANAGEMENT OF CHRONIC WOUNDS

In order to discuss factors that interfere with normal acute wound healing and result in a chronic wound, it is important to understand how normal acute wound healing occurs. Injury to skin starts a cascade of events to repair the defect. This healing process occurs in phases. Each of the phases occurs in consecutive order and overlaps with the previous phase. We have attached a series of slides (Attachment 1) that are included with this paper which compliments the information in these written comments. The first slide addresses the order of normal wound healing phases as stated below:

- **Hemostasis - 10 mins** the body's first response to injury and the phase in which clot formation occurs to prevent bleeding. This phase occurs over a period of minutes and results in the initial release of the inflammatory cytokines and growth factors from the platelet into the wound bed to initiate the healing response.
- **Inflammation – 2-5 days** this phase follows the onset of hemostasis. The primary functions of inflammation are to remove bacteria and debris (to prevent infection) and to stimulate cells necessary for the next phase of healing. During inflammation, many cells are summoned. However two of the main cells are neutrophils and macrophages (Wound Care Essentials, p 62). Inflammation normally lasts only a few days.
- **Proliferation – 2 days-3 weeks** during this phase the major activity focuses on angiogenesis (new blood vessel formation) and granulation tissue formation (scar tissue for full-thickness wounds). It is also during the proliferative phase that wound contraction and epithelialization occur.
- **Remodeling – 6 months-2 years** is the final phase of healing. During remodeling (also known as maturation) the collagen fibers in the scar are reorganized to improve tensile strength. Remodeling can last up to 18 months. Scar tissue is 30% less strong than the original tissue.

Most chronic wounds that fail to heal are "stuck" in the inflammatory phase of the normal healing process. In this inflammatory phase—which follows the normal clotting and vascular response phases—neutrophils and macrophages are attracted to the wound site where they secrete large quantities of a variety of enzymes, including matrix metalloproteinases (MMPs) and elastases, that break down damaged matrix. As invading microbes and damaged tissues are cleared, inflammatory cells present in the wound are cleared, the recruitment of inflammatory cells ends, and inflammation subsides. This is followed by the formation of new blood vessels, the synthesis of collagen and other extracellular proteins, re-epithelialization, contraction, and ultimately scar formation. *The presence of bioburden and biofilm impedes the normal healing process by continuously stimulating immune-mediated inflammation within the wound leading to a negative cycle of chronic inflammation and tissue damage.* The wound is unlikely to progress unless this barrier to wound healing is removed.

Slides 2 and 3 address "What is Biofilm" and "Impact of bioburden and infection on wound healing."

Therefore, when physicians or clinicians assess and manage a chronic wound, they will use the following clinical observations and interventions relating to wound bed preparation. In 2003, this concept of wound bed management was created using the acronym of TIME and is grouped into four areas, all of which need to be addressed at each wound assessment:

- *Tissue:* assessment and debridement of non-viable or foreign material (including callus, host necrotic tissue, adherent dressing material, multiple organism-related biofilm or slough, exudate and debris) on the surface of the wound.
- *Infection/inflammation:* assessment of the etiology of each wound, need for topical antiseptic and/or systemic antibiotic use to control infection and management of inappropriate inflammation unrelated to infection.
- *Moisture imbalance*: assessment of the etiology and management of wound exudate.
- *Edge of wound:* assessment of non-advancing or undermined wound edges (and state of the surrounding skin).

The fourth and last slide addresses the clinical observations, intervention and clinical outcome for each one of these approaches. We have also attached the article, "Extending the TIME concept: what have we learned in the Past 10 Years?" Leaper DJ, Schultz G, Carville K, Fletcher J, Swanson T, Drake R. Int. Wound J 2012; 9 (Suppl. 2):1–19, which will give more detailed information about these processes. (Attachment 2)

MANAGEMENT OF CHRONIC WOUNDS USING ANTIMICROBIAL WOUND CARE PRODUCTS

As stated above, to get the chronic wound to progress in healing, the biofilm and bioburden needs to be removed. There are many ways to manage bioburden, infection and biofilm– debridement, antimicrobial wound care products, and antibiotics. The treatment is multi-faceted. Debridement is an effective way to remove dead tissue and debris, it also exposes bacteria in a biofilm making them more susceptible to antimicrobials.

Antimicrobial wound care products are an important tool for managing chronic wounds. They can act as bacterial barriers to minimize bacterial ingress or egress from a wound helping to minimize spread of bacteria; in addition they can reduce bioburden within a dressing and are important as part of the multi-faceted management strategy of wound bed preparation, including preventing bacterial/ biofilm re-growth after debridement. Two articles which we have attached address the small window of time that one has to use a bacterial barrier to reform mature biofilms:

- The article "Biofilm maturity studies indicate sharp debridement opens a time-dependent therapeutic window," [iv]states that biofilms can reform on wounds in about 3 days if a bacterial barrier dressing is not used after sharp debridement.
- In a 2010 article "Biofilms made Easy" [v]it is stated that wounds "rapidly recover from mechanical disruption and reform mature biofilm within 24 hours."

In addition, topical antimicrobials such as silver provide broad spectrum antimicrobial activity against bacteria and fungi. They usually act against multiple targets within the microbial cells (Cell walls/ membrane, proteins, DNA) minimizing the chance of resistance development.

So when do clinicians decide to use an antimicrobial wound care product when they are treating a chronic wound? As we will describe in our presentation during the Panel meeting, clinicians decide to use antimicrobial wound care products when a wound fails to progress even if co-morbidities are managed and the wound exhibits evidence of increased bioburden.

Two sets of guidelines by Alliance members Association for Advancement in Wound Care (AAWC) and Wound Ostomy Continence Nurses Society (WOCN) address the need for using antimicrobial wound care products.

In its pressure ulcer and/or its venous ulcer guidelines, the AAWC state the following:

When wound progression is not evident within the first weeks of standard treatment or there is documented bacterial overload, use of topical antimicrobial products with known safety profiles effective against gram-negative, gram-positive and anaerobic organisms, e.g. with safe, sustained release of ionic silver, iodine or other agents with evidence of safety on chronic wounds are recommended.[vi]

- Adjunctive wound management with antiseptic or antimicrobial dressings is supported in clinical guidelines for pressure ulcer and venous ulcer care.[vii]
- The activity level of the antimicrobial ingredients is contained locally at the wound site and not absorbed into the systemic system.
- Products with antiseptics or antimicrobials are used for limited periods of time, until the wound begins to develop new granulation tissue.
- Once healing progression is evident on a continuous basis, antimicrobial products are replaced with products that do not contain the antiseptic or antimicrobial component that are appropriate for the specific wound condition.
- Guidelines suggest these products be assessed at least every two weeks for continued clinical use.

These guidelines are supported by the following publications:

- **Consider systemic antibiotic use only on VU with clinical signs of infection: A** (O'Meara et al., 2010)
- **Cadexomer iodine dressings improves healing on clinically infected wounds: A** (Hansson, et al., 1998; O'Meara et al., 2010)
- **Silver-containing foam or collagen/oxidized regenerated cellulose dressings: A**(Dimakakos et al., 2009; Jørgensen et al, 2005; Munter et al., 2006)

The WOCN state in its Pressure Ulcer Guideline[viii]: For antimicrobial dressings/silver and honey dressings: Consider a two week course of topical antibiotics for clean pressure ulcers that do not heal or continue to produce purulent exudate after two to four weeks of standard care."

Additional guidelines produced by the European Wound Management association (EWMA) suggest "that there is an urgent need for the use of antimicrobial treatment regime that does not include antibiotics" [ix]

More recently, a group of wound care experts published a consensus document [x] addressing the appropriate use of silver in wounds – highlighting the benefits of silver on wound bioburden, and providing clinical guidance on when and when not to use silver and for how long.

PRODUCTS CLASSIFIED IN THE FRO PRODUCT CATEGORY, THEIR INDICATIONS FOR USE AND TESTING

The Alliance reviewed the over 400 products currently listed in the FRO category and found the category contains many diverse product groups with different indications for use as identified in their 510ks. They include both OTC and prescription products as well. The products could be categorized as follows:

- Antimicrobial dressings and gels that contain such ingredients as silver, honey, polyhexamethlene biguanide (PHMB)—some are used for management of wounds and others for catheter sites
- Antimicrobial wound care solutions that are used for cleansing, irrigating, moistening, and debriding- to remove wound debris from acute and chronic dermal lesions that are partial or full thickness wounds- and that contain such ingredients as: hypochlorous acid (HCIO) and silver.
- Dressings that are indicated for management of wounds but do not contain antimicrobials
- Saline solutions
- Hemostatic agents
- Ointments, creams that are used to manage and relieve the signs and symptoms of seborrhea and seborrheic dermatitis
- Other products that contain such ingredients as sucralfate/hydrochloric acid and are used for the management of pain and relief of pain by adhering to the mucosal surface of the mouth and soothing oral lesions.

In reviewing the indications for use (IFU) for these various groups, we found them to be diverse to all be included in the same FRO category. However, the IFUs were consistent for similar types of products. For example:

- The antimicrobial wound care dressings IFUs were all very similar in that they all claim that the product is used in the MANAGEMENT of a type of wound not in TREATING THE WOUND. Some examples are:
    - Indicated for the management of moderate to heavily exuding wounds by providing a moist environment, which is conducive to wound healing, and supports and aids autolytic debridement.
    - Indicated for management of light to heavy exudating wounds.

- For the antimicrobial wound care solutions, the IFUs stated they are used:
    - to moisten the wound bed and facilitate autolytic debridement of acute and chronic dermal lesions/ relieves itch and pain associated with dermal irritation, sores, injuries and ulcers of dermal tissue in addition to moistening and lubricating absorbent wound dressings/indicated for the management of partial or full thickness wound
    - for management and moisturizing of wounds.

For many of the OTC products the IFU states:

- may be used for abrasions, minor cuts, etc.
- intended for OTC use for management of minor skin abrasions, minor lacerations, minor irritations, minor cuts, and intact skin.

Currently, the products in the FRO category are cleared through 510ks. The current approach of the manufacturers of these devices is to use bench testing and animal studies to establish that they are as safe and as effective as those already in the market, and we believe that is has proven to be sufficient controls for these low to moderate risk device types.

Our recommendation is that these product be classified into class II category and continue to require 510k clearance. The FDA may want to consider whether there may be some appropriately placed in Class I and exempt from 510k for example those that are OTC and comprised of well characterized agents.

EVIDENCE FOR SAFETY AND EFFECTIVENESS OF PRODUCTS IN FRO CATEGORY/ LOW RISK OF ANTIMICROBIAL RESISTANCE

Given the long history of the use of many of the products that are in the FRO category, the Alliance believes that there is no need to re-establish their safety or efficacy. The benefits of their use outweighs their well understood risks and there are publications to support these conclusions. In terms of safety, we have reviewed the MAUDE data from 2015- 2016 and found that there are no new significant risks identified; that is, that there were no reports that patients have developed any severe systemic infections or that there was an increase in serious adverse events associated with these products. In addition, the manufacturers of these products have indicated that in their

monitoring over the years of product use there are no emerging issues related to of patients developing systemic infections or risks of bacterial resistance.

We appreciate the importance of appropriately addressing the risk of antimicrobial resistance for the subset of those products that contain antibiotics. The use of terminology here is very important and many terms are used to describe these products; therefore we are defining these terms based on the FDA definitions:

- Antimicrobial agents are substances that kill or inhibit the growth of microorganisms. In many instances in which the antimicrobial acts outside the body, such as antimicrobial sterile drapes and gloves used in patient procedures, FDA does not treat the antimicrobial as a drug. FDA has regulated such products as devices rather than combination products. Today these products meet many of the general requirements for combination products.

http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm071396.pdf

- Antibiotics- FDA's definition of antibiotics is a subset of antimicrobials- often known as antimicrobial drugs, are drugs that fight infections caused by bacteria- http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/antibioticsandantibioticresistance/default.htm
    - Antiseptics- Health care antiseptics are antimicrobial agents that are intended to reduce the number of micro-organisms on the skin. They prevent the grow http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/economicanalyses/ucm447035.pdf)

The types of antibiotics that are used topically or systemically in infected wound treatment include drugs such as tetracycline, erythromycin, neomycin, polymyxin-B, doxycycline, Bacitracin, Gentamycin, Mupirocin, Silver sulfadiazine, Tobramycin, Ciprofloxacin.

However, after reviewing the products in the FRO category, we don't believe that any of these antibiotics are included in it; therefore, there is a low risk of inducing resistance to these important antibiotics with the use of the FRO wound care products.

Many products in the FRO category do however contain silver. After decades of use of silver wound care products, we are unaware of any journal report where there was development of silver resistant organisms due to the use of silver containing wound care products. We believe that any current data is insufficient to consider this a significant public health problem at this time. In the article, "The increasing use of silver-based products as antimicrobial agents: a useful development or a cause for concern?" Dr. Chopra states that .. even though silver resistance has been documented, current evidence suggests the clinical threat is low." [xi]Silver has been used in wound care for many decades without serious problems.

ADDITIONAL ISSUES FOR FDA CONSIDERATION

The Alliance met with FDA staff in July 2015 to discuss our issues and recommendations for updating the 2006 Guidance for Industry Chronic Cutaneous Ulcer and Burn Wounds – Developing

Products for Treatment document. We would like to reiterate some of the points we made during our productive meeting.

As mentioned above, we believe that the appropriate type of data for wound care products that are Class II are bench tests and animal studies to address their ability to control colonization taken from the claims. However, we believe that the FDA should consider alternative clinical endpoints that may need to be defined for new antibiotic therapies that might be considered PMA products based on unknown risks of inducing resistance. We would appreciate the opportunity to discuss this further with the FDA staff.

In addition, at the same July 2015 meeting the Alliance addressed the following:

- Value of voluntary registries to understand how and when wound care products are used and the complex management of wounds such as:
    - The strong external validity of registries is achieved by the fact that they include "typical patients," unlike RCTs
    - Registry data can provide a good description of the course of a disease and impact of interventions in actual practice
    - May be more relevant to decision making than the data derived from individual clinical trials
    - ***"Even though registries have more opportunities to introduce bias (systematic error), well designed observational studies can approximate the effects of interventions as well as RCTs on the same topic, and in particular, in the evaluation of health care effectiveness. "(AHRQ – Registries for Evaluating Patient Outcomes – A Users Guide 3rd Edition, Chapter 10.1 Generalizability)T***
    - How and why registries are used:
        - Observe the course of a disease
        - estimate magnitude of a problem, determine incidence, assess service delivery, document types of patients served by providers, describe or estimate survival)
        - Understand variations in treatment and outcomes
        - Determine clinical effectiveness, cost effectiveness or comparative effectiveness
        - Including the acceptability of drugs, devices or procedures for reimbursement
        - Monitor safety
        - Measure or improve quality of care

- Concerns with the FDA terminology for different product classifications
    - Currently 510(k) and PMA biological, cellular and/or tissue based products for skin wounds have been put into FDA product classifications indicating that they are "wound dressings."
    - "Wound dressing" terminology used for these product categories is outdated and cannot represent the true nature of these products.
    - Many of the products are resorbed in the body, and some are temporary.
    - In practice "Wound dressing" is usually used to mean inert temporary coverings.

- Many payers have been confused with FDA labeling CTPs as "wound dressings"; payers thus believe they are topically applied protective covers and pay them as part of an office visit E&M service
- CTP products are applied surgically, most with an associated debridement or excision prior to their application.
- **Recommendation:** Biologicals regulated as devices product classification titles should be changed to better represent the nature of these products.

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On behalf of the Alliance of Wound Care Stakeholders, we appreciate the opportunity to submit these comments. If you have any questions or would like further information, please do not hesitate to contact me.

Sincerely,

Marcia Nusgart R.Ph.
Executive Director

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[i] Sen, Chandan K. et al "Human skin wounds: A major and snowballing threat to public health and the economy." Wound Rep Reg. 2009 17 p. 764.

[ii] Kerstein MD. The non-healing leg ulcer: peripheral vascular disease, chronic venous insufficiency, and ischemic vasculitis. Ostomy Wound Manage. 1996; 42(10A Suppl):19S-35S.

[iii] Hingorani, Anil et al, The management of the diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine, Journal of Vascular Surgery, February Supplement 2016, 3S-21S

[iv] Wolcott R.D. et al Biofilm maturity studies indicate sharp debridement opens a time-dependent therapeutic window. Journal of Wound Care Vol 19, No, 8 August 2010

[v] Phillips P.L. et al, Biofilms Made Easy, Wounds International 2010

[vi] Association for the Advancement of Wound Care (AAWC) Guideline of Pressure Ulcer Guidelines. Malvern, Pennsylvania: Association for the Advancement of Wound Care (AAWC) 2010.

[vii] Ibid, Association for the Advancement of Wound Care (AAWC) Venous Ulcer Guideline. Malvern, Pennsylvania: Association for the Advancement of Wound Care (AAWC).December 2010. Accessible at http://aawconline.org/professional-resources/resources/

[viii] Wound Ostomy Continence Nurses Society Pressure Ulcer Guidelines 2003

[ix] Gottrup, F., Apelqvist, J. & Bjansholt, T. EWMA Document: Antimicrobials and Non-healing Wounds—Evidence, Controversies and Suggestions. *J Wound Care* **22,** S1–S92 (2013)

[x] Ayello, E.A.et al International Consensus, Appropriate use of silver dressings in wounds. An expert working consensus London: Wounds International 2012)
[xi] Chopra, Ian, "The increasing use of silver-based products as antimicrobial agents: a useful development or a cause for concern?" Journal of Antimicrobial Chemotherapy 2007

Attachments:

- Attachment 1-
  - Slide1- Normal Wound Healing
  - Slide 2- What is a Biofilm?
  - Slide 3- Impact of Bioburden and Infection on Wound Healing
  - Slide 4- Wound Bed Preparation

- Attachment 2- " Leaper DJ, Schultz G, Carville K, Fletcher J, Swanson T, Drake R. Int. Wound J 2012; 9 (Suppl. 2):1–19

- Attachment 3- Wolcott R.D. et al Biofilm maturity studies indicate sharp debridement opens a time-dependent therapeutic window. Journal of Wound Care Vol 19, No, 8 August 2010

- Attachment 4- Phillips P.L. et al, Biofilms Made Easy, Wounds International 2010