COALITION OF

Wound Care Manufacturers

November 21, 2016

Janice M. Soreth, M.D.
Associate Commissioner for Special Medical Programs
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane Room 1061
Rockville, Maryland 20852

Submitted electronically to Evella.Washington@fda.hhs.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 Dr. Soreth;

On behalf of the Coalition of Wound Care Manufacturers ("Coalition"), I am pleased to submit follow-up comments in response to the September 20-21, 2016 Food and Drug Administration's (FDA) meeting of the General and Plastic Surgery Devices Panel ("Panel") of the Medical Devices Advisory Committee. The Coalition submitted on September 1, 2016 its first set of comments before the Panel meeting. The Coalition represents leading manufacturers of wound care products used by Medicare beneficiaries for the treatment of wounds. This Panel meeting was of particular interest to us as many of our members manufacture antimicrobial wound care products which were the subject of these discussions.

The Coalition is in agreement with the recommendations of the General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee to the FDA that antimicrobial wound care products (i.e., Solid Wound Dressings combined with Drugs and Wound Dressings combined with Drugs formulated as a Cream, Gel, or Ointment) should be classified in Class II with special controls. Antimicrobial wound products are used for the management of wounds in general, not for the treatment of infected wounds. There are wound dressings combined with drugs with significant history and levels of clinical experience, including data from clinical trials and literature published in peer-reviewed journals.

We believe these products are low to moderate risk and have been shown to be safely used in the marketplace for many years. The Coalition also agrees with the FDA's use of multiple product classification categories for antimicrobial products currently regulated in the FRO category (i.e., solids, cream/gel/ointment and liquid washes) and believe that

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the Agency should develop a guidance document as a special control to support the classification and indications for use and claims for these medical devices.

SPECIFIC COMMENTS

Antimicrobial products in the FRO Category should be classified into Class II and be reviewed by FDA under the 510(k) program

Class II Classification is Appropriate for Wound Management Products

As you know, FDA assigns premarket review of a combination product based on its primary mode of action, which for the wound management products under discussion is the device mode of action.[1] As such, the premarket review of the wound management products is assigned to the Center for Devices and Radiological Health, and is subject to the device premarket review framework. As this class of products were on the market well before 1976, they have been subject to the 510(k) requirement, akin to most Class II products, under the FRO product code.

To be a Class II product, a combination of general and special controls should be sufficient to provide reasonable assurance of safety and effectiveness. Often the special controls come in the form of specific testing requirements for 510(k) submissions. These controls have essentially been established over time through 510(k) review standards, as discussed in more detail, below.

The 510(k) premarket notification process has been demonstrated to be an effective tool to regulate wound dressings combined with drugs in the FRO category. Clearance is based upon substantial equivalence to a lawfully marketed predicate, with a significant amount of data included in the 510(k) for these product lines. Testing can include:

- Cytotoxicity Evaluations
- Primary Skin Irritation Study
- Acute Dermal Toxicity Study
- Acute Systemic Toxicity
- Intracutaneous Toxicity
- Sensitization Study
- Chronic Toxicity Studies In Vitro Microbiology Activity
- Kinetic Studies for the release of the antimicrobial from the wound dressing
- *In Vitro* Zone of Inhibition Studies
- Bench Testing
- Animal Testing
- Clinical Testing
- Risk Analysis/Risk Mitigation/Risk Management

[1] *See* 21 C.F.R.Part 3.

In every case where a product was cleared in the FRO category, FDA has evaluated the data and other information and decided the product is at least as safe and effective as other lawfully marketed wound management products. When one considers the decades that these products have been used, and the absence of signals suggesting safety or effectiveness problems (as detailed in the comments of the Alliance of Wound Care Stakeholders), and have been subject to numerous evaluations, this provides a significant level of assurance regarding to the safety and effectiveness for products on the market today.

We also would like to emphasize that that consistent with the above analysis, these products fail to meet the standards for high, Class III, product classification. A Class III classification would require findings that –

1. Insufficient information exists to determine that general and/or special controls are sufficient to assure a reasonable assurance of safety and effectiveness for the uses that are intended (e.g., described in labeling), and
2. The product
    a. Is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or
    b. Presents a potential unreasonable risk of illness or injury.

Neither of these criteria is met. With regard to (1), in light of the information discussed above, it has been shown that 510(k) data expectations for the FRO category are sufficient to provide reasonable assurance of safety and effectiveness, and can be adopted as special controls with a Class II. With regard to (2), although wound management products are important to health, this criterion is generally met only by products where product failures would likely result in serious injury or death, such as pacemakers and certain cancer diagnostics. Wound management products do not fall within these categories of high-risk products

Wound Management and Wound Healing Indications Must be Distinguished

During the Panel meeting, there was discussion of the clinical indications for antimicrobial wound care dressings. To clarify, antimicrobial wound care dressings are generally intended to contribute to ***wound management***, not to treat or heal the wound by their use alone. The specific claims made in the labeling for these products commonly include: maintain a moist wound environment, covers and protects the wounds, provides a barrier to penetration of microbes to the wound, which may reduce the risk of infection, to enhance the microbial barrier function and minimize growth of microbes in the wound dressing, minimize contamination/colonization of the dressing. For these and similar wound management claims, the data that are currently required by FDA provide a reasonable assurance for the safety and effectiveness of the products.

The Coalition firmly believes that each of these performance characteristics for products with the typical claims above can be supported using bench testing. For example, specific to the bacterial barrier and microbial colonization, in vitro methods exist which simulate clinical use and are capable of demonstrating the ability of the dressing to prevent external contamination and reduce bioburden in the dressing.

We would like to point out that, as outlined in FDA's Executive Summary and in the Panel meeting, the General and Plastic Surgery Devices Panel had an Advisory Panel meeting in August 2005. FDA presented information on dressings that contained drugs, silver, bismuth, chlorhexidine, and others, including risk of use, risk mitigation measures. The Panel voted unanimously to recommend that FDA classify wound dressings with a drug as Class II with special controls and we are in agreement with that decision then and also at the recent Panel meeting.

Antimicrobial Dressings in the FRO Category are Low to Moderate Risk in Terms of Safety and There is No Evidence that They Have Significantly Contributed to the Problem of Antibiotic Resistance

Antimicrobial wound care dressings in this category have been reviewed for market entry via 510(k) for 40 years, with a history of 40 years of safe and effective use under this process (and much longer if you consider historical pre-1976 use of these products). These products have a long, well understood history of clinical usage, their risks are known and characterized and can be well controlled with appropriate testing, similar to what the manufacturers perform today in support of clearance for these products, as noted above.

As regards antibiotic resistance, we would like to clarify that these antimicrobial wound care products that contain such ingredients as silver, honey, cadexomer iodine and PHMB are antiseptics and do not appear to contribute to antibiotic resistance, nor would they be expected to be given that they can work via a different mechanism of action than antibiotics. For instance, in his presentation at the Panel meeting, Dr. Randall Wolcott explained that antibiotics mainly have a narrow spectrum of activity (against specific types of bacteria) and usually act on one target in the cell. Silver ions, on the other hand, bind to multiple targets on bacterial and fungal cells which reduce the chance of resistance development.

We note that at the Panel meeting, Dr. Finn Gottrup, the guest speaker, stated that “honey and the iodine has never been shown to give, as well as I know, any resistant bacteria”. Also, after decades of use of silver containing wound care products, the Coalition is unaware of any published journal report where development of silver resistant organisms due to the use of silver containing wound care products was documented. These antimicrobial wound care dressings are distinct from antibiotic dressings or ointments

that contain bacitracin or mupirocin which are used to treat infections and are not used to manage chronic wounds in the same way as the products being considered for classification.

Issues Regarding Clinical Practice Guidelines and Clinical Evidence

The Coalition would like to highlight a limitation to the discussion of the clinical practice guidelines referenced in the Panel meeting and their recommendations with regards to the use of antimicrobial dressings. Many of the guidelines that were presented did not evaluate or consider the use of antimicrobial dressings. The chart (pg. 63) that illustrated the guidelines stated, incorrectly, that antimicrobial dressings were not recommended in situations where the products considered were actually antibiotics or antibiotic dressings.

Therefore, for some indications, the use of these dressings was not recommended within the guidelines for routine care or uninfected wounds. The lack of a recommendation does not necessarily correlate with a recommendation against the use of these dressings in these situations. We understand that the Alliance of Wound Care Stakeholders (of which the Coalition is a member) will be providing more detail on the focus of these guidelines and identify additional guidelines that do recommend the use of antimicrobial dressings in specific clinical situations. In addition, Coalition members will be providing in their own comments, the scientific evidence to support the use of their antimicrobial wound care dressings for their current claims.

In conclusion, antimicrobial wound care dressings currently in the FRO category should be classified as Class II medical devices and regulated using the 510(k) premarket notification process. We further recommend that an FDA guidance document regarding wound dressings with drugs, for products like those currently regulated in the FRO category, be developed for use as the special control required for this class.

The Coalition appreciates the opportunity to provide our comments. If you need further information or have any questions, please do not hesitate to contact me.

Sincerely,

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Senior Policy Advisor