

04 October 2016*Medical Device Alert*

On September 20 and 21, 2016, FDA convened an Advisory Panel to obtain recommendations regarding the appropriate regulatory classification for wound dressings containing drugs. Such devices are widely used to treat medical conditions ranging from minor cuts and burns, to diabetic foot ulcers. These devices—including those containing antimicrobial agents intended to prevent microbial growth on the device—historically have been cleared to market through the 510(k) process under product code FRO as unclassified, pre-amendments devices. While this is not the first time FDA has looked to outside experts to help evaluate the classification of wound dressings that contain drugs¹, this most recent panel meeting was prompted by several factors, including the recent evolution in technology, the breadth of the cleared indications for use of these devices, the extensive list of ingredients (many with known or potential chemical activity), and the public health implications associated with antimicrobial resistance (as evidenced by FDA's recent ban of 19 antibacterial agents in soaps²). Much of the Panel discussion about the appropriate regulation of wound dressings that contain drugs was largely consistent with the current regulatory scheme. However, the Panel believed that increased scrutiny and regulation may be necessary for certain forms of these products, particularly those including antibiotics, to prevent the continued rise of antimicrobial resistance.

At the meeting, the Panel specifically discussed the clinical use and regulatory considerations for three sub-categories of wound dressings that contain drugs:

- solid wound dressings such as bandages and gauzes;
- gels, creams, and ointments; and
- liquid wound washes

The central consideration to this discussion was the purpose of the drug as applied to the dressing. As combination products, wound dressings that contain drugs are regulated by the Center for Devices and Radiological Health (CDRH) under FDA's medical device authorities if their primary mode of action is that of a medical device—otherwise, the combination would be regulated by the Center for Drug Evaluation and Research (CDER) under FDA's drug authorities. Clearance of wound dressings with drugs via the 510(k) process has, to date, been premised on the drug component being intended to prevent the growth of microorganisms on the device itself, rather than impacting the patient directly. Indeed, under this premise, FDA promulgated 21

C.F.R. § 878.4015 classifying *Wound Dressing with Poly(diallyl dimethyl ammonium chloride) (pDADMAC) Additive* as class II devices.³ As with other cleared wound dressing with drugs, these devices are intended to act as a physical barrier to outside contaminants and are not intended to act on the surface or interior of the wound. Special controls were developed and published in a guidance document to outline the data requirements for a 510(k) application. The guidance explicitly states that the device does not contain antimicrobial agents that act on the body and that the guidance is not applicable for those products in which the pDADMAC leaches from the substrate. Leachability testing is required to be submitted in the 510(k) notice for these devices to demonstrate that the drug does not leach onto the patient.

Following the reasoning set forth above, the Panel agreed that class II is generally appropriate for solid wound dressings containing drugs; however, products including antimicrobial agents were thought to deserve additional consideration. In some cases, particularly where antimicrobial agents are used that could lead to increased antimicrobial resistance or toxicity if improperly administered, the panel members recommended classification into class III to permit a more detailed review of the antimicrobial agents in the context of a PMA.

While the Panel's analysis was relatively straight-forward for solid wound dressings, the intended use of antimicrobial agents added to wound dressings in the form of gels, creams, ointments, and liquid wound washes was considerably less clear. Antimicrobial agents included in these specific formulations of wound dressings are ostensibly intended to prevent the growth of microbes on the product or on the packaging. There are arguably other methods, such as use of preservatives, to achieve this goal. The Panel considered the clinical value of adding drugs to the product and whether they should be added at all. The Moderator drove this point home by asking the Panel: "Are these products a Trojan horse to deliver drugs to the patient?" Notably, neither FDA nor the Panel members appeared to share this concern as a general matter, but remained focused on controlling the use of antibiotics and other compounds linked with antimicrobial resistance.

Following two days of discussions and deliberations, in the end, the Panel generally recommended that wound dressings with drugs, whatever their form, be regulated as class II devices, while products with certain antimicrobial drugs that may be harmful to the patient or bolster antimicrobial resistance, such as antibiotics should be regulated as class III products. While this recommendation is generally in-line with FDA's existing approach to the regulation of wound dressing containing drugs, the Panel meeting raised important regulatory considerations as it relates to the drug component in these products and the impact of these considerations on the regulatory status of the product – namely whether the drug is intended to act on the device itself and whether or not it leaches onto the patient. Undoubtedly, under this rubric, FDA will require leachability and stability data in any 510(k) notice for such products going forward. For liquid, cream, or gel wound dressings, however, the Panel deliberations were less definitive and seemed to suggest that there may be some support for considering these types of wound dressings as drug delivery systems, which would subject them to regulation by CDER under FDA's drug authorities.

Taking into consideration the discussions and the recommendations made at the Panel meeting, FDA plans to develop a regulatory path forward for the broad category of products currently regulated as class II wound dressings containing drugs. Given the Panel's comments on the purpose and the safety risk of adding certain drugs to wound dressings, we would anticipate that this process will be a collaborative effort between CDRH and CDER going forward. Companies that currently market these products, or that are developing products in this space, should carefully consider these recent developments, the regulatory considerations raised at the Panel meeting, and the possible increased scrutiny of certain of these products going forward.

1 At a similar meeting in 2005, the Panel unanimously recommended that FDA classify these products as class II devices.

2 See <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm378393.htm>

3 See

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocumentResources>

<http://www.fda.gov/AdvisoryCommittees/Calendar/ucm515104.htm>

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDe>

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