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Wound Products, Antimicrobial Resistance, and Commercial Speech: FDA's Solution in Search of a Problem

by Jennifer Newberger

To borrow (at least in part) from Shakespeare, "FDA doth protest too much, methinks" when it comes to its proposed rule that would impose more stringent regulatory controls of wound products. These protestations begin with FDA maintaining that wound products with antimicrobials may contribute to global concerns about antimicrobial resistance (AMR), continue on with discussions of whether, despite decades of use, there is adequate evidence of clinical utility, and, for the finale, conclude with FDA's attempt to strip manufacturers of the ability to use certain words or phrases to describe their products-language that, for many products, has been used for decades.

In the end, the proposed rule seems to be a solution in search of a problem—a solution raising, at minimum, violations of the Administrative Procedure Act (APA) as well as the commercial speech protections provided by the First Amendment of the United States Constitution.

How Did We Get Here?

The beginning is a very good place to start.

On May 28, 1976, the Medical Device Amendments (MDA) went into effect, establishing medical devices as a class of products distinct from drugs. The MDA required FDA to classify device types on the market at that time into Class I (low risk), Class II (moderate risk), or Class III (high risk). Depending on the classification, products would be subject to different levels of regulatory oversight. Ultimately what FDA established was a process by which most Class I devices do not require premarket review by FDA prior to commercialization. Class II devices, for the most part, are authorized for marketing through the 510(k)-clearance process. This process requires a showing of "substantial equivalence" to a legally marketed device. These devices may also be subject to what is known as "special controls," usually in the form of testing or labeling requirements. Class III devices are authorized through a premarket approval (PMA) application, nearly always requiring a well-controlled clinical study. As FDA went through the classification process, products that remained unclassified came to market through the 510(k) process and a showing of substantial equivalence to devices marketed prior to enactment of the MDA.

By this point, FDA has classified most device types. Most, but not all. Solid wound dressings, wound dressings formulated as gels, creams, or ointments, and liquid wound washes (collectively, "wound products") have not, to this date, been classified. FDA has been regulating these as Class II devices through the 510(k)-clearance process for nearly 50 years, and for wound products with drugs, has created the product code FRO. Hundreds of products have been cleared under FRO—so many, in fact, that it is difficult to assess the precise number because the 510(k) database will not

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provide a result greater than 500. In a 2016 meeting held to discuss classification of FRO products, FDA indicated the number at that time was around 700.

FDA is finally getting around to formally classifying these wound products, as it is well within their legal authority to do. FDA has held two advisory panel meetings to discuss the appropriate classification of wound products with antimicrobials—in August 2005 and September 2016. In 2005, the panel unanimously agreed that wound products with antimicrobials should be regulated as Class II devices with special controls.[1]

Perhaps not liking the answer it received, FDA never issued a formal classification based upon the recommendation of the 2005 panel, and instead called another panel in 2016. That panel in fact acknowledged that the prior panel had recommended putting wound dressings with antimicrobials into Class II, and asked FDA why it was calling another panel. FDA did not specifically address why it failed to act at that time, noting only that science and medicine had changed over the prior 11 years. In the 2016 panel meeting, FDA was intent on focusing on antimicrobial resistance, other potential risks to health, whether adequate clinical data existed to support the safe use of the products, and what special controls would be appropriate, with an emphasis on labeling claims.[2]

The Proposed Rule

Antibiotic "Risk." Seven years after the most recent panel meeting, FDA finally decided it was time to classify wound products with antimicrobials. In a proposed rule published on November 30, 2023, FDA put forth a split classification, stating that wound products containing "medically important antimicrobials," namely antibiotics, pose a high AMR risk, and therefore should be classified into Class III. Wound products with medium- or low-level AMR concern would remain in Class II, subject to new special controls.[3]

More specifically, FDA stated: "High-level of AMR concern results from wound dressings and liquid wound washes that contain a medically important antimicrobial as these products **may** directly contribute to the development and spread of organisms in the patient that are resistant to medically important antimicrobials."[4] There are two notable take-aways from this position. First, the use of the word "may"—FDA seems to be basing a conclusion for upclassification of certain products based not on solid scientific evidence that use of these products leads to AMR, but rather on a possibility that their use "may" lead to this outcome. Presumably FDA uses this softer language because there is no solid scientific evidence tying these wound products to the "development and spread of organisms in the patient that are resistant to medically important antimicrobials."

Not only did FDA *not* provide any evidence to support this position, but one could also argue it provides data to support the opposite. FDA discusses recalls associated with the wound products, noting that it reviewed recalls reported for these products from 2003 through July 2022. Notably, **there were no recalls for solid wound dressings, wound dressings formulated as a gel, cream, or ointment, or liquid wound washes containing medically important**

[1] *See* FDA, Brief Summary from the General and Plastic Surgery Devices Panel Meeting (Aug. 25-26, 2005), https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/GeneralandPlasticSurgeryDevicesPanel/ucm124755.htm.

[2] *See* FDA, 2016 Meeting Materials of the General and Plastic Surgery Advisory Panel (Sept. 20-21, 2016), https://www.fda.gov/advisory-committees/general-and-plastic-surgery-devices-panel/2016-meeting-materials-general-and-plastic-surgery-advisory-panel.

[3] Medical Devices; General and Plastic Surgery Devices; Classification of Certain Solid Wound Dressings; Wound Dressings Formulated as a Gel, Creams, or Ointment; and Liquid Wound Washes, 88 Fed. Reg. 83,774, 83,775 (Nov. 30, 2023).

[4] *Id.* at 83,778 (emphasis added).

antimicrobials during this timeframe.[5] None, in nearly 20 years. One would think that if these products were leading to increased morbidity and mortality, some recalls certainly would have been conducted.

Not only does FDA appear to lack any scientific evidence supporting the need to upclassify wound products with medically important antimicrobials (antibiotics), but doing so would not appear to solve the alleged problem. While it is reasonable to expect that not all manufacturers of these types of wound products would necessarily pursue PMA approval, there is nothing that would preclude them from doing so. If they went through the PMA process and received the approvals, the products, with all their supposed AMR risks, would remain on the market. We are therefore left to believe that somehow, if these products are still on the market, but as PMAs rather than 510(k)s, they will be less likely to lead to AMR. This conclusion lacks all sense and logic.

The only reasonable takeaway is that FDA knows full well what the result of this rule would be, if finalized—manufacturers of wound dressings with antibiotics will not pursue PMAs, leading to fewer products on the market, thereby potentially reducing the (unproven) AMR risk associated with them. If FDA's true concern was the level of AMR resulting from these products, it would need to take them off the market altogether. Since its ability to remove products from the market is very narrow, it is using the cover of pre-amendments status and the need for formal classification to achieve its goal.

FDA attempts to justify its actions by tying its decision to the 2016 panel called to discuss classification of wound products with antimicrobials. As with its other justifications, this also appears to leave FDA flat-footed. FDA's characterization of the 2016 panel is that a majority agreed that Class III was appropriate for wound products with antibiotics. A review of the transcript shows otherwise. Of the 14 panel members, seven said that all FRO products should remain in Class II, two said all should go to Class III, and five indicated that most should remain in Class II, other than those with antibiotics, which should be in Class III. Thus, FDA implying that its decision is due to the feedback from the 2016 panel is merely an attempt to deflect its own responsibility over the process.

Perhaps FDA's greatest error is one of omission. The proposed rule is predicated on high levels of AMR risk presented by wound products containing antibiotics, leading a reasonable reader to conclude that there are many such products on the market. The transcript to the 2016 panel tells a different story. In response to a question about the volume of these products, FDA stated its belief that there were fewer than five cleared wound products with antibiotics in them. Five, out of over 700. The logical question—though one never raised at the panel or addressed in the proposed rule—is how much AMR risk those five products could actually be causing, in light of the hundreds of other products available on the market. Thus, FDA's conclusion that products with antibiotics are posing such a dire risk to the public health that they must be classified in Class III is arbitrary, capricious, an abuse of discretion, and unsupported by substantial evidence; in other words, a perfect decision for an APA challenge.

Special Controls. For the Class II devices that will continue to make up most of the wound products with antimicrobials, FDA is proposing the imposition of special controls. Some of these, such as performance testing and biocompatibility evaluation, are standard and already part of the 510(k) submissions for these products. Others, however, are likely to impose burdens so great that they may be impossible to fulfill. For example, FDA is now requiring manufacturers to conduct an AMR risk assessment in order for a wound product with antimicrobials to be cleared. The proposed

[5] *Id.* at 83,787.

rule provides no insight into how a sponsor might make this showing, or what the threshold will be. As discussed above, given the lack of any clear evidence explicitly tying use of these particular products to a risk of AMR, the imposition of this special control without any information as to what it will mean for future submissions is also ripe for a legal challenge.

While there are many other special controls imposed, perhaps most disturbing are the labeling controls, specifically intended to prohibit truthful speech of the manufacturers. To explain its rationale, FDA provides a confusing and incorrect description of how a product would be deemed a combination product rather than a device. In particular, FDA stated that use of the phrase "wound management" previously resulted in wound products being deemed combination products, rather than devices. Per FDA, "[t]his was because the term 'wound management' could be interpreted broadly, encompassing uses not only including to cover and protect a wound, to absorb exudate, and to maintain appropriate moisture balance, but also uses such as treatment of wounds/wound infection."[6]

FDA is essentially stating that a product could be deemed a combination product rather than a device (or, presumably, a drug) depending on how a claim "could" be interpreted, rather than its physical make-up. The basis for this interpretation is puzzling, given that the regulatory definition of a combination product has nothing to do with how a claim "could" be interpreted, but is clearly dependent on the composition of the product. A combination product is defined as "a product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity."[7] Therefore, a physical barrier, such as a solid wound dressing, that contains an antimicrobial drug product, is a combination product, regardless of its claims. There should be no question about this.

How the product is regulated—as a drug or device—turns on the primary mode of action—a question of science, not of claims. FDA, however, is maintaining that by simply saying "wound management" the product cannot be regulated as a device. Taken to its logical conclusion, the results of this position are nonsensical. Wound products, with or without antimicrobials, do, in fact, help to "manage" wounds, by protecting them, absorbing exudate, or irrigating them. This protective or cleansing action is therefore a device action, but FDA will no longer allow this truthful claim, should the rule be finalized. FDA's position that it will deem a product a combination product or device based solely on how a claim "could" be interpreted is not based anywhere in the law.

Considering "wound management" as the determiner of product status is just the beginning. According to FDA, not only is "wound management" confusing from a product classification standpoint, it is also potentially misleading, since "it is not consistently used and is unclear from a clinical perspective."[8] Therefore, FDA states that the term "'wound management' be replaced with the specific functions of the wound dressing and liquid wound washes (e.g., cover and protect the wound in the case of solid wound dressings)."[9]

Manufacturers are well within their legal rights to describe their product truthfully, even if the term is not "consistently used" or "clear from a clinical perspective." Those requirements are not in the statute or the regulations, and, to our knowledge, are different standards than have been imposed on other products. Wound management has long been used to describe the purpose of

[6] *Id.* at 83,785.

[7] 21 C.F.R. § 3.2(e)(1).

[8] 88 Fed. Reg. at 83,786.

[9] *Id.*

these wound products, and can be done in a truthful, non-misleading manner. FDA has no legal authority to issue this type of blanket prohibition on speech, especially as it relates to a term that it has long permitted for this product type.

FDA's next word on the chopping block is "may." Yes, in this proposed rule FDA states that the word "may" is ambiguous and "could mislead the end users when describing a specific use (e.g., 'may reduce the risk of infection')."[10] FDA proposes that, instead, "intended uses, indications, and claims should be clearly stated and supported by appropriate data."[11] While this is laughable for many reasons, the utmost of these is that FDA itself uses the word "may" to justify the need for this rule. As you ~~may~~ recall, at the beginning of this article we discussed FDA's statement, "High-level of AMR concern results from wound dressings and liquid wound washes that contain a medically important antimicrobial as these products **may** directly contribute to the development and spread of organisms in the patient that are resistant to medically important antimicrobials." We can only assume that FDA's position is that "may" is not ambiguous when it uses the term, but only when used by product sponsors. As with "wound management," this type of absolute prohibition, in this case against a word used by the agency itself and frequently throughout the English language, has no legal, scientific, or logical support whatsoever.

These prohibitions are a blatant violation of the First Amendment's protection of commercial speech, which is presumed protected if the speech is lawful and not misleading. In considering whether a government's restriction on speech is permissible, a court would consider whether the government's interests are substantial. Assuming the answer to be yes, the next question is "whether the regulation directly advances the governmental interest asserted, and whether it is not more extensive than is necessary to serve that interest."[12] In the case of this proposed rule, these speech prohibitions are more extensive than necessary to serve FDA's interest in protecting the public's health. If manufacturers make false or misleading claims about their products, FDA may take enforcement action. It can ask for additional data or a new clearance to support the claim. It may not make blanket prohibitions against speech for an entire class of products when such speech "may" in fact be truthful and non-misleading for products within the class.

For all these reasons, FDA's proposed rule regarding wound products is arbitrary, capricious, not based on substantial evidence, and a violation of the protections afforded commercial speech under the First Amendment. FDA must reconsider this rule and ensure that any solution is scientifically and constitutionally sound.

[10] *Id.*

[11] *Id.*

[12] *Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n of New York,* 447 U.S. 557, 566 (1980).

