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Client Alert

FDA and Life Sciences

JANUARY 10, 2024

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FDA Issues Proposed Rule Classifying Certain Wound Dressings and Liquid Wound Washes For the First Time

After enactment of the Medical Device Amendments of 1976, which established three regulatory classes for medical devices, the Food and Drug Administration (FDA) has been required to classify all medical devices into Class I, II, or III. However, in the nearly 50 years since, FDA has failed to classify various types of wound dressings and liquid wound washes containing antimicrobials and other chemical protectants or preservatives. These wound dressings and liquid wound washes typically are cleared for marketing by FDA through the 510(k) premarket notification process as Unclassified, pre-Amendments devices.

In 1998, 2005, and 2016, the General and Plastic Surgery Devices Panel of FDA's Medical Devices Advisory Committee held meetings to consider the proposed classification of these devices. On November 30, 2023, FDA published a proposed rule that for the first time would classify certain external cutaneous (skin) wound dressings and liquid wound washes with antimicrobials and/or other chemical preservatives. Products with an antimicrobial associated with a high level of antimicrobial resistance (AMR) concern would be considered Class III devices, while products with a chemical or an antimicrobial associated with a medium or low level of AMR concern would be considered Class II devices, subject to certain special controls.

This client alert focuses on the key features of the proposed rule and the timing for its potential implementation, to provide a basic understanding of FDA's proposal. If finalized, the proposed rule would impact skin wound dressings and liquid wound washes that are already marketed, along with new market entrants.

PROPOSED RULE: CLASSIFICATION SCHEME

If finalized, the proposed rule, "*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*" (Proposed Rule),[i] would classify skin wound dressings and washes containing antimicrobials and/or other chemicals. FDA excludes from the Proposed Rule a skin wound dressing or liquid wound wash that meet any one of the following criteria: (i) does not contain an antimicrobial or "other chemicals"[ii]; (ii) contains a topical analgesic; (iii) contains hydrocortisone; (iv) is intended to provide hemostasis; (v) is intended for the reduction or prevention of catheter-related infection; (vi) is intended for use on the mucosa; (vii) is already classified in a classification regulation; or (viii) achieves its intended use through chemical action or is a combination product.

FDA proposes to classify skin wound dressings and liquid wound washes with antimicrobials and/or other chemicals into three separate classification regulations: (1) solid wound dressings; (2) wound dressings formulated as a gel, cream, or ointment; and (3) liquid wound washes. A common feature of each category is the dividing line between placement of a product in Class III versus Class II. Specifically, under the Proposed Rule, a product would either be Class III or Class II with special controls depending on whether FDA considers the antimicrobial(s) in the product to pose a high, medium, or low level of antimicrobial resistance (AMR) concern. FDA defines levels of antimicrobial resistance (AMR) concern as follows:

- 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, potentially further limiting a clinician's therapeutic options.
- Medium-level AMR concern results from wound dressings and liquid wound washes that contain a nonmedically important antimicrobial which may indirectly select for organisms with medically important antimicrobial resistance mechanisms via coselection mechanisms such as coresistance and cross-resistance.
- Low-level AMR concern results from wound dressings and liquid wound washes that contain a nonmedically important antimicrobial which lacks the ability to coselect for organisms with medically important antimicrobial resistance mechanisms.[iii]

FDA defines ''medically important antimicrobial" by reference to a 2018 publication by the World Health Organization (WHO) which defines three classes (critically important, highly important, or important) of medically important microbials.[iv] If the WHO has deemed an antimicrobial to be critically important, highly important, or important, then FDA deems it to be a "medically important antimicrobial" for purposes of the Proposed Rule.

The Proposed Rule provides examples from each category: polymyxin B, silver sulfadiazine, and bacitracin pose a high-level of AMR concern and therefore the products containing one or more of these antimicrobials (if not excluded as described previously) would be placed in Class III; silver, zinc, copper, chlorhexidine, and benzalkonium chloride pose a medium-level AMR concern and therefore products containing one or more of these antimicrobials (if not excluded as described previously) would be placed in Class II; and parabens hypochlorous acid, peroxide, polyhexamethylene biguanide (PHMB), and iodine containing products pose a low-level of AMR concern and therefore would be placed in Class I. To be marketed, Class III products would require an approved premarket application (PMA), whereas Class II products would require 510(k) clearance and compliance with a variety of special controls defined in the Proposed Rule. Required special controls would include performance testing, antimicrobial characterization and performance testing, and specified labeling.[v] Class I products are typically exempted from 510(k) clearance.

SOLID WOUND DRESSINGS

Under the Proposed Rule, the regulation for solid wound dressings would be promulgated in 21 C.F.R. § 878.4016, "Solid wound dressings containing antimicrobials and/or other chemicals." These products would be identified as follows:

a) *Identification*. A solid wound dressing containing antimicrobials and/or other chemicals that are in a category listed in paragraph (a)(2) of this section is used to cover and protect a wound, to absorb exudate, and to maintain appropriate moisture balance within the wound and is intended for use only on external cutaneous (skin) wounds. The solid wound dressing materials are resorbable or nonresorbable, synthetic or naturally derived materials (including animal-derived materials such as collagen or chitosan), which are provided sterile in a form able to hold structural integrity temporarily or permanently. This regulation does not include a solid wound dressing that contains only animal-derived materials without the presence of antimicrobials and/or other chemicals.

   1) Antimicrobials are used for protectant purposes only to reduce microbial growth within the solid wound dressing while in use, or to provide an antimicrobial barrier to microbial penetration through the solid wound dressing;

   2) Categories of other chemicals are wound protectants, honey, synthetic peptides, or botanical extracts.[vi]

WOUND DRESSINGS FORMULATED AS A GEL, CREAM, OR OINTMENT

The regulation for gel, cream, or ointment wound dressings would be promulgated in 21 C.F.R. § 878.4017, "Wound dressings formulated as a gel, cream, or ointment containing antimicrobials and/or other chemicals." These products would be identified as follows:

a) *Identification*. A wound dressing formulated as a gel, cream, or ointment containing antimicrobials and/or other chemicals that are in a category listed in paragraph (a)(2) of this section is used to maintain appropriate moisture balance within the wound and is intended for use only on external cutaneous (skin) wounds. The wound dressing materials are synthetic or naturally derived materials (including animal-derived materials such as collagen or chitosan). Wound dressings formulated as a gel, cream, or ointment containing antimicrobials and/or other chemicals are amorphous and can have high water content with thickening agents or consist of an oil-water emulsion. This regulation does not include a wound dressing formulated as a gel, cream, or ointment that contains only animal-derived materials without the presence of antimicrobials and/or other chemicals.

   1) Antimicrobials are used for preservative purposes only to maintain shelf life for a nonsterile wound dressing or a multiple-use wound dressing for single patient use only;

   2) Categories of other chemicals are wound protectants, honey, synthetic peptides, or botanical extracts.[vii]

LIQUID WOUND WASHES

The regulation for liquid wound washes would be promulgated in 21 C.F.R. § 878.4019, "Liquid wound washes." These products would be identified as follows:

a) *Identification*. A liquid wound wash containing antimicrobials and/or other chemicals that are in a category listed in paragraph (a)(2) of this section is a water-based solution used to mechanically irrigate and physically remove debris from external wounds and intended for use on external cutaneous (skin) wounds. It is also used to

moisten solid wound dressings to maintain appropriate moisture balance within the dressing. This regulation does not include liquid wound washes that contain only animal-derived materials without the presence of antimicrobials and/or other chemicals.

1) Antimicrobials are used for preservative purposes only to maintain shelf life for a nonsterile liquid wound wash or a multiple-use liquid wound wash for single patient use only;

2) Categories of other chemicals are wound protectants, honey, synthetic peptides, or botanical extracts.[viii]

COMBINATION PRODUCTS

Under the Federal Food, Drug, and Cosmetic Act (FDCA), a product is a device only if it achieves its primary purposes via means that do not include chemical or metabolic action.[ix] A commonality of the three proposed regulations is that the role of the antimicrobial is limited to acting as a preservative and/or product protectant. FDA considers these intended uses to constitute a device-only mode of action. In particular, the intended use of the antimicrobial is defined in a manner that, according to FDA, clarifies that it is acting as a device and not as a drug. Therefore, the products falling within the three proposed classification regulations would be considered devices and not combination products.

Although not stated in the Proposed Rule, the preamble conveys the message that a product that makes express or implied claims, or claims for antimicrobials outside these three regulatory identifications, regarding the function of the antimicrobial (other than as a preservative or protectant) may be considered a combination product or a drug. If so, according to the preamble, such products would not be within the scope of the Proposed Rule. For instance, FDA suggests that a "wound management" indication could potentially create an intended use that would result in the product being considered a combination (i.e., drug-device) product or drug product that is outside the scope of the Proposed Rule. If a wound dressing or wash with an antimicrobial is deemed to be a combination product, then, under established rules, it would be regulated primarily as a drug or device based upon its primary mode of action. The Office of Combination Products (OCP) has final authority for making these determinations.[x]

EFFECTIVE DATES

Per FDA, the Proposed Rule will become effective 30 days after publication of a final rule in the *Federal Register*.[xi] Also, FDA concurrently published a proposed order that would require the filing of a PMA within 30 months of the effective date for any product within scope of the Proposed Rule that would be in Class III; the failure to file a PMA in this timeframe would render the device adulterated.[xii] The Proposed Order, however, states that FDA does not intend to enforce compliance with the 30-month deadline for currently marketed products if a notice of intent to file a PMA is submitted within 90 days of the effective date of the final order.[xiii] If this notice is submitted, then FDA proposes to grant an additional 90 days for submission of a PMA past the 30-month deadline. Further, manufacturers may continue marketing their product during FDA's review of a PMA. If the manufacturer receives a not approvable or denial determination, then marketing must cease.

With regard to Class II products, FDA states in the Proposed Rule that it would accept a new 510(k) and would issue a new clearance letter, as appropriate, indicating substantial equivalence and compliance with the special controls. These devices could serve as predicates for new devices. These clearance letters would be made publicly available in FDA's 510(k) database, and compliance with special controls at the time of clearance would be noted in the publicly available 510(k) Summary posted in this database.[xiv] FDA does not state whether it is requiring new 510(k)s, but it also states that if a device is marketed without obtaining a new 510(k) clearance, FDA proposes that it must be brought into compliance with special controls 6 months after the effective date of the rule, when finalized, and would be subject to

the “usual” enforcement policies if it is not. For new entrants, 510(k) clearance based upon demonstrated compliance with the applicable special controls would be required within six months of the effective date of the final rule.[xv]

For marketed products to be placed in Class III, FDA cites to a clear statutory mechanism requiring PMA approval after a grace period to replace their current 510(k) clearance. For marketed products to be placed in Class II, the legal basis for FDA’s position is not clear, as FDA does not cite to any parallel statutory mechanism requiring a new 510(k) clearance for lawfully marketed devices to replace their current 510(k) clearance. The special controls appear to focus on information to be provided in a new 510(k) submission. It is not clear how they could or would be enforced against marketed devices; FDA’s reference to applying its “usual” enforcement policies does not shed much light on this question.[xvi]

Additionally, FDA emphasizes that the Proposed Rule classifies only the subset of legally marketed unclassified wound dressings and wound washes, i.e., devices falling within one of the classification regulations quoted above. If a currently unclassified device, lawfully on the market pursuant to 510(k) clearance, does not fit within these regulatory definitions (*e.g.*, it has antimicrobials but also a broad “wound management” intended use), then it is not clear whether the Proposed Rule applies to it; if not, the device would remain unclassified and lawfully marketed pursuant to its existing 510(k).

Finally, in the preamble, FDA indicates that marketed wound dressings and liquid wound washes with antimicrobials that otherwise do not fit within the classifications promulgated by the Proposed Rule may be considered either (i) a combination product regulated by CDER or CDRH based on the product’s primary mode of action, or (ii) a drug regulated by CDER. As FDA acknowledges, that would be a case-by-case determination based upon many factors, such as the product labeling and the amount of antimicrobial contained in the product (e.g., some amounts of microbial may be objectively beyond what is necessary to preserve the product).

CONCLUSION

There is much more to the Proposed Rule than we could cover in this short analysis. Comments on the Proposed Rule are due February 28, 2024. If you have questions or would like assistance drafting and submitting a comment, please do not hesitate to contact us.

[i] 88 Fed. Reg. 83,774 (Nov. 30, 2023) [hereinafter "*Proposed Rule*"].
[ii] Plant-derived materials that are highly purified (e.g., cellulose) or well-characterized (e.g., cotton) are not considered "other chemicals." *Id*. at 83,778.
[iii] *Id.* at 83,778.
[iv] *See id.* (referencing WHO, *Critically Important Antimicrobials for Human Medicine: 6th Edition*, Table 1 (2018)).
[v] *See id.* at 83,797-98.
[vi] *Id.* at 83,796-97.
[vii] *Id.* at 83,798.
[viii] *Id.* at 83,800.
[ix] *See* FDCA § 201(h), 21 U.S.C. § 321(h).
[x] *See* 21 C.F.R. Part 3.
[xi] *Id.* at 83,792.
[xii] *See* FDA, Proposed Order, *Effective Date of Requirement for Premarket Approval Applications for Certain Solid Wound Dressings; Wound Dressings Formulated as a Gel, Cream, or Ointment; and Liquid Wound Washes Containing Medically Important Antimicrobials*, 88 Fed. Reg. 83,802 (Nov. 30, 2023) [hereinafter "*Proposed Order*"].
[xiii] *See id.* at 83,805.
[xiv] *See Proposed Rule*, 88 Fed. Reg. at 83,793.
[xv] *See id.*
[xvi] *Id. at 83793.*