area which may result in impaired wound healing.

(vii) Any statements in the labeling must be clear such that they may be understood by the end user, supported by appropriate evidence, and consistent with the intended use of mechanically irrigating a wound or maintaining appropriate moisture balance within a solid wound dressing.

Dated: November 21, 2023.

Robert M. Califf,

Commissioner of Food and Drugs.

[FR Doc. 2023–26209 Filed 11–29–23; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 878

[Docket No. FDA–2023–N–3275]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed amendment; proposed order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is proposing to require the filing of a premarket approval application (PMA) for certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing antimicrobials with a high level of antimicrobial resistance (AMR) concern (*i.e.,* medically important antimicrobials) acting as either protectants or preservatives, which are unclassified, preamendments devices. FDA is summarizing its proposed findings regarding the degree or risk of illness or injury designed to be eliminated or reduced by requiring the devices to meet the PMA requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and the benefits to the public from the use of the devices.

DATES: Either electronic or written comments on the proposed order must be submitted by February 28, 2024. FDA intends that, if a final order based on this proposed order is issued, anyone who wishes to market solid wound dressings, wound dressings formulated as a gel, cream, or ointment, and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives must submit a PMA prior to the last day of the 30th calendar month beginning after the month in which the classification of the device in class III became effective. See section III for the effective date of any final order that may publish based on this proposed order. See section VI of this document for more information about submitting a PMA.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of February 28, 2024. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov*.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2023–N–3275 for ''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.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Brandon Kitchel, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4626, Silver Spring, MD 20993–0002, 301–796–6055, *brandon.kitchel@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background—Regulatory Authorities

The FD&C Act, as amended, establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three classes of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three classes of devices are class I (general controls), class II (special controls and general controls), and class III (premarket approval and general controls). Under section 513(d)(1) of the FD&C Act, devices that were in commercial distribution before the enactment on May 28, 1976 of the 1976 amendments (Medical Device Amendments of 1976, Pub. L. 94–295) (generally referred to as ''preamendments devices'') are classified after FDA has (1) received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

A person may market a preamendments device that has been classified into class III through premarket notification procedures, without submission of a PMA until FDA issues an administrative order under section 515(b) of the FD&C Act (21 U.S.C. 360e(b)) requiring premarket approval.

Section 515(f) of the FD&C Act provides an alternative pathway for meeting the premarket approval requirement. Under section 515(f), manufacturers may meet the premarket approval requirement if they file a notice of completion of a product development protocol (PDP) approved under section 515(f)(4) of the FD&C Act and FDA declares the PDP completed under section 515(f)(6)(B) of the FD&C Act. Accordingly, the manufacturer of a preamendments class III device may comply with a call for PMAs by filing a PMA or a notice of completion of a PDP. In practice, however, the option of filing a notice of completion of a PDP has rarely been used. For simplicity, although the PDP option remains available to manufacturers in response to a final order under section 515(b) of the FD&C Act, this document will refer only to the requirement for filing and obtaining approval of a PMA.

Section 515(b)(1) of the FD&C Act sets forth the process for issuing a final order. Specifically, prior to the issuance of a final order requiring premarket approval for a preamendments class III device, the following must occur: (1) publication of a proposed order in the **Federal Register;** (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act; and (3) consideration of comments from all affected stakeholders, including patients, payors, and providers.

Section 515(b)(2) of the FD&C Act provides that a proposed order to require premarket approval shall contain: (1) the proposed order; (2) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA, and the benefit to the public from the use of the device; (3) an opportunity for the submission of comments on the proposed order and the proposed findings; and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

Section 515(b)(3) of the FD&C Act provides that FDA shall, after the close of the comment period on the proposed order,[1] consideration of any comments received, and a meeting of a device classification panel described in section 513(b) of the FD&C Act, issue a final order to require premarket approval or publish a document terminating the proceeding together with the reasons for such termination. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the FD&C Act, unless the reason for termination is that the device is a banned device under section 516 of the FD&C Act (21 U.S.C. 360f).

A preamendments class III device may be commercially distributed without a PMA until 90 days after FDA issues a final order requiring premarket approval for the device, or 30 months after the classification of the device in class III under section 513 of the FD&C Act becomes effective, whichever is later (section 501(f)(2)(B) of the FD&C Act (21 U.S.C. 351(f)(2)(B)). Elsewhere in this issue of the **Federal Register**, FDA is proposing to classify solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing antimicrobials with a high level of AMR (*i.e.,* the ability of a microorganism to resist the effects of an antimicrobial) concern to class III. Therefore, if the proposed classification regulation and the order to require PMAs are finalized at the same time, a PMA for these wound dressings must be filed within the 30-month period because that will be the later of the two time periods. If a PMA is not timely filed for such devices, then the device would be deemed adulterated under section 501(f) of the FD&C Act.

Also, a preamendments device subject to the order process under section 515(b) of the FD&C Act is not required to have an approved investigational device exemption (IDE) (see part 812 (21 CFR part 812)) contemporaneous with its interstate distribution until the date identified by FDA in the final order requiring the filing of a PMA for the device. At that time, an IDE is required only if a PMA has not been filed. If the manufacturer, importer, or other sponsor of the device submits an IDE application and FDA approves it, the device may be distributed for investigational use. If a PMA is not filed by the later of the two dates, and the device is not distributed for investigational use under an IDE, the device is deemed adulterated within the meaning of section 501(f)(1)(A) of the FD&C Act and subject to enforcement action.

II. Regulatory History of the Devices

After the enactment of the Medical Device Amendments of 1976, FDA undertook an effort to identify and classify all preamendments devices, in accordance with section 513(d) of the FD&C Act. Consistent with the FD&C Act, FDA has held multiple General and Plastic Surgery Devices Panel meetings regarding the classification of wound dressings: on November 27, 1998 (Ref. 1); August 25 and 26, 2005 (Ref. 2); and September 20 and 21, 2016 (the 2016 Panel) (Ref. 3). However, only the 2016 Panel meeting provided the class III recommendations. Certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials (*i.e.,* antimicrobial drugs that are important for therapeutic use in humans and associated with a high level of AMR concern) pose different risks than other

[1] In December 2019, FDA began adding the term ''Proposed amendment'' to the ''ACTION'' caption for these documents to indicate that they ''propose to amend'' the Code of Federal Regulations. This editorial change was made in accordance with the Office of the Federal Register's interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

wound dressings. Elsewhere in this issue of the **Federal Register**, FDA is proposing to classify certain unclassified, preamendments solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials into class III. A PMA, in addition to general controls, will provide reasonable assurance of the safety and effectiveness of these devices.

The proposed rule would also establish the identification, classification, and regulatory controls for certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes that contain antimicrobials acting as either protectants or preservatives with a medium or low level of AMR concern and/or other chemicals. These devices have been subject to premarket review through a 510(k) submission and have been cleared for marketing if FDA considers the device to be substantially equivalent to a legally marketed predicate in accordance with section 513(i) of the FD&C Act. To date, FDA has cleared more than 500 of these devices and has cleared only one of the device types that we believe will be subject to the PMA requirements.

On September 20 and 21, 2016, the 2016 Panel met for the purposes of obtaining recommendations about the classification of products, including (1) solid wound dressings; (2) wound dressings formulated as a gel, cream, or ointment; and (3) liquid wound washes (Ref. 3). FDA held the 2016 Panel to obtain input on the risks to health and benefits of wound dressings and liquid wound washes that contain antimicrobials and/or other chemicals, as well as the clinical relevance of certain indications. The 2016 Panel was asked to recommend to FDA whether such wound dressings and liquid wound washes that contain antimicrobials and/or other chemicals should be classified into class III (subject to premarket approval), class II (subject to general and special controls), or class I (subject only to general controls). The 2016 Panel was also asked to discuss the types of evidence (including clinical evidence) that would be helpful to support certain indications, as well as appropriate controls necessary to mitigate the risks to health and assure the safety and effectiveness of these types of wound dressings and liquid wound washes.

For solid wound dressings containing antimicrobials and/or other chemicals, the 2016 Panel reviewed the list of risks to health and potential mitigation measures provided by FDA and agreed that the list was acceptable. In general, a majority of the 2016 Panel recommended that solid wound dressings should be classified into class II, subject to special controls, with the exception of certain solid wound dressings containing antimicrobials, such as antibiotics (with similar consideration to antimicrobial agents that may select for resistance in indirect ways). Some of the 2016 Panel believed all wound dressings and liquid wound washes containing antimicrobials and/or other chemicals should be classified as class III because of the absence of high-quality evidence of benefit; others recommended class III be considered for any product containing an antibiotic or an antimicrobial that may indirectly contribute to antibiotic resistance.

For wound dressings containing antimicrobials and/or other chemicals formulated as a gel, cream, or ointment, the 2016 Panel reviewed the list of risks to health and potential mitigation measures provided by FDA and agreed that the list was acceptable. In general, a majority of the 2016 Panel recommended that wound dressings formulated as a gel, cream, or ointment should be classified into class II, subject to special controls, with the exception of certain wound dressings formulated as a gel, cream, or ointment containing antimicrobials, such as antibiotics (with similar consideration to agents that may select for resistance in indirect ways), for which some members of the 2016 Panel recommended class III.

For liquid wound washes containing antimicrobials and/or other chemicals, the 2016 Panel reviewed the list of risks to health and potential mitigation measures provided by FDA and agreed that the list was acceptable. In general, a majority of the 2016 Panel recommended that liquid wound washes should be classified into class I or class II, subject to special controls, depending on the toxicity of the product, with the exception of certain liquid wound washes containing antimicrobials, such as antibiotics (with similar consideration to agents that may select for resistance in indirect ways), for which some members of the 2016 Panel recommended class III.

The 2016 Panel recommended that wound dressings and liquid wound washes with medically important antimicrobials [2] (Ref. 4) be classified into class III because there was a lack of available evidence to determine that general and special controls are sufficient to provide reasonable assurance of safety and effectiveness, and these devices present a potential unreasonable risk of illness or injury. FDA agrees with the 2016 Panel's recommendation. It is also FDA's position that there is a lack of available evidence to determine that general and special controls are sufficient to provide reasonable assurance of the devices' safety and effectiveness and that the devices present a potential unreasonable risk of illness or injury. FDA further agrees with the 2016 Panel's recommendation that wound dressings and liquid wound washes with medically important antimicrobials and/or other chemicals be classified into class III subject to PMA.

III. Dates New Requirements Apply

If FDA finalizes the proposed classification of certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives, these devices will be classified into class III. In accordance with sections 501(f)(2)(B) and 515(b) of the FD&C Act, FDA is proposing to require that a PMA be filed with the Agency for certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives by the last day of the 30th calendar month beginning after the month in which the classification of the device in class III became effective.

An applicant whose product was legally in commercial distribution before May 28, 1976, or whose product has been found to be substantially equivalent to such a product, will be permitted to continue marketing such class III product during FDA's review of the PMA, provided that a PMA is timely filed. FDA intends to review any PMA for the device within 180 days. FDA cautions that under section 515(d)(1)(B)(i) of the FD&C Act, the Agency may not enter into an agreement to extend the review period for a PMA beyond 180 days, unless the Agency finds that ''. . . the continued availability of the device is necessary for the public health.''

[2] Table 1 of the World Health Organization's (WHO) 2018 publication ''Critically important antimicrobials for human medicine: 6th revision'' (*https://www.who.int/publications/i/item/9789241515528*) has a list of all classes of medically important antimicrobials. For the purposes of this proposed order, an antimicrobial is considered medically important if, and only if, it falls within any of these classes regardless of the level of importance specified by the WHO (*i.e.,* critically important, highly important, or important).

Moreover, manufacturers must cease distribution of devices upon receiving a not approvable or denial decision rendered on a PMA. In such circumstances, to resume distribution, these manufacturers must receive PMA approval for their devices. However, the product may be distributed for investigational use only if the requirements of the investigational device exemptions regulations in part 812 are met. The requirements for investigational use of significant risk devices include submitting an IDE application to FDA for review and approval. An approved IDE is required to be in effect before an investigation of the device may be initiated or continued under 21 CFR 812.30. FDA, therefore, recommends that IDE applications be submitted to FDA at least 30 days before the date a PMA is required to be filed to avoid interrupting investigations.

For currently marketed wound dressings and liquid wound washes that are proposed to be classified into class III, FDA is proposing that it does not intend to enforce compliance with the 30-month deadline by which PMAs must be submitted, when a notice of intent to file a PMA is submitted within 90 days of the effective date of the order, if finalized. In circumstances when a notice of intent to file is submitted, FDA is proposing that it does not intend to enforce compliance with the 30-month deadline by which PMAs must be submitted when a PMA is submitted within 90 days after the 30-month deadline. However, as discussed above, even if a notice of intent and PMA are submitted by these dates, manufacturers must cease distribution of devices upon receiving a not approvable or denial decision rendered on a PMA.

IV. Devices Subject to This Proposal

A solid wound dressing containing antimicrobials and/or other chemicals is used to cover and protect a wound, to absorb exudate, and to maintain appropriate moisture balance within the wound. Medically important antimicrobials that are incorporated in the solid wound dressing 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.

A wound dressing formulated as a gel, cream, or ointment containing antimicrobials and/or other chemicals is used to maintain appropriate moisture balance within the wound. Medically important antimicrobials that are incorporated in a wound dressing formulated as a gel, cream, or ointment are used for preservative purposes only to maintain shelf life for a non-sterile wound dressing or a multiple-use wound dressing for single patient use only.

A liquid wound wash is a water-based solution used to mechanically irrigate and physically remove debris from external wounds. It is also used to moisten solid wound dressings to maintain appropriate moisture balance within the dressing. Medically important antimicrobials that are incorporated in a liquid wound wash are used for preservative purposes only to maintain shelf life for a non-sterile liquid wound wash or a multiple-use wound wash for single patient use only.

FDA currently regulates these unclassified devices as devices requiring a 510(k) submission under product codes FRO, GER, MGP, MGQ, and EFQ.

Elsewhere in this issue of the **Federal Register**, FDA is proposing to classify certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives in class III and identifies these devices as follows: solid wound dressings containing antimicrobials and/or other chemicals; wound dressings formulated as a gel, cream, or ointments containing antimicrobials and/or other chemicals; and liquid wound washes.

In accordance with section 515(b)(2)(D) of the FD&C Act, interested persons are being offered the opportunity to comment or request a change on the Agency's proposed classification of certain solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives based on new information published elsewhere in this **Federal Register**.

V. Proposed Findings With Respect to Risks and Benefits for Solid Wound Dressings; Wound Dressings Formulated as a Gel, Cream, or Ointment; and Liquid Wound Washes Containing Medically Important Antimicrobials

As required by section 515(b) of the FD&C Act, FDA is publishing its proposed findings regarding: (1) the degree of risk of illness or injury designed to be eliminated or reduced by requiring that these devices have an approved PMA and (2) the benefits to the public from the use of the devices. These findings are based on the reports and recommendations of the 2016 Panel, and any additional information that FDA has obtained. Additional information regarding the risks can be found below, as well as in the proposed rule published elsewhere in this issue of the **Federal Register**, proposing to classify these devices into class III.

Based on this information, FDA has identified the following risks to health to the different categories of wound dressings and liquid wound washes that are within the scope of this proposed rule and classification action:

- *Solid Wound Dressings*:
  - Adverse tissue reaction, immunological reaction, transmission of pathogens and parasites, toxicity, delayed wound healing, incompatibilities with other therapies, contribution to the spread of AMR, infection, microbial growth within the product, product degradation during stated shelf storage, loss of barrier function, retention of dressing material in wound, and negatively impacting the skin microbiota in the peri-wound area resulting in impaired wound healing.
- *Wound Dressings Formulated as a Gel, Cream, or Ointment:*
  - Adverse tissue reaction, immunological reaction, transmission of pathogens and parasites, toxicity, delayed wound healing, incompatibilities with other therapies, contribution to the spread of AMR, infection, microbial growth within the product, product degradation during stated shelf storage, and negatively impacting the skin microbiota in the peri-wound area resulting in impaired wound healing.
- *Liquid Wound Washes*:
  - Adverse tissue reaction, immunological reaction, transmission of pathogens and parasites, toxicity, delayed wound healing, incompatibilities with other therapies, contribution to the spread of AMR, infection, microbial growth within the product, product degradation during stated shelf storage, inability to remove wound debris and foreign materials, and negatively impacting the skin microbiota in the peri-wound area resulting in impaired wound healing.

Below is a brief description of each of the identified risks to health:

- *Adverse tissue reaction:* Erythema, irritation, inflammation of the wound or host tissue, immune response, and hemolysis can occur as a result of an unwanted tissue response associated with the materials or leachables/extractables in wound dressings and liquid wound washes.
- *Immunological reaction:* This can result from a device derived from a new animal source or protein denaturation/

modification due to the manufacturing conditions.

- *Transmission of pathogens and parasites* (*e.g.,* bacteria, mycoplasma, fungi, viruses, and other transmissible spongiform encephalopathy agents): This can result from contaminated animal sources, feed, inadequate processing, and viral inactivation of the animal-derived materials.
- *Toxicity:* Local and/or systemic toxicity, tissue necrosis, reduced tissue viability, and genotoxicity can occur due to toxic antimicrobials or other chemicals in the wound dressings or liquid wound washes, which can result in adverse tissue effects, leading to toxicity. This also includes allergic reaction and sensitization, as individuals with known sensitivity to the materials in the wound dressings and liquid wound washes may experience allergic reactions, which may be severe depending on the degree of sensitivity.
- *Delayed wound healing:* Cytotoxicity resulting in dead or necrotic tissue can delay healing.
- *Incompatibilities with other therapies:* An undesirable (*e.g.,* antagonistic) reaction could occur between the materials contained in/on the wound dressings or liquid wound washes and other therapies applied to the wound.
- *Contribution to the spread of AMR:* Use of antimicrobials in wound dressings and liquid wound washes can inadvertently select for and cultivate antimicrobial resistant organisms in patients and further limit a clinician's therapeutic options to treat infections.
- *Infection:* Unsafe methods of manufacturing processes, such as inadequate aseptic processing, inadequate packaging and/or product storage, can result in contaminated product that may be a source of infection. This risk includes bacterial and fungal infections and superinfections, which may result from the use of an antimicrobial-containing wound dressing or liquid wound wash that introduces contaminating microorganisms to the wound or disrupts the natural balance of skin flora around the wound.
- *Microbial growth within the product:* This can occur from inadequate sterilization, preservative effectiveness failure, unsafe methods of manufacturing processes, inadequate packaging and/or product storage. This can lead to a change in product composition or characteristics (*e.g.,* loss of tensile strength, change in pH) and may also result in infection or adverse tissue reaction.
- *Product degradation during stated shelf storage:* Inadequate packaging and/or inappropriate storage of wound dressings or liquid wound washes can result in product degradation during storage. Product degradation can also change the composition or characteristics of the product over time and lead to patient harm.
- *Retention of dressing material in wound:* This risk is generally applicable to solid wound dressings, which can occur due to a loss in solid dressing integrity or unintended degradation of solid wound dressings. It may also occur due to the healthcare provider inadvertently leaving material in the wound. This can lead to adverse tissue reaction, delay in wound healing, or infection.
- *Inability to remove wound debris and foreign materials:* Ineffective washing of the wound can occur. Debris and foreign material remaining in the wound can delay healing or lead to infection. This risk is applicable to the liquid wound washes containing antimicrobials and/or other chemicals.
- *Loss of barrier function:* This risk is applicable to solid wound dressings indicated as barriers to microbial penetration through the wound dressing (either via mechanical or antimicrobial properties). Loss of this barrier function can introduce microbial contamination from the environment into the wound and can lead to delay in wound healing or infection.
- *Impact to skin microbiota in the peri-wound area:* This risk is applicable to each category of antimicrobial-containing wound dressings. Inadvertent leaching of antimicrobials away from the dressing may negatively impact the skin microbiota in the peri-wound area by reducing the presence of beneficial commensal microorganisms that play a role in the wound healing cascade, resulting in impaired wound healing.

A. Summary of Data

FDA conducted queries of the Manufacturer and User Facility Device Experience database to identify adverse events related to use of solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives. The queries resulted in the identification of 1,973 Medical Device Reports (MDRs) on these devices as of July 21, 2022. The reports were received by FDA from 1994 to July 21, 2022. The number of MDRs received between 1994 and 2004 were consistently low, at fewer than 20 per year. Between 2005 and 2016, the number of MDRs increased to an average of 111 reports per year with a peak in 2015, at 298 MDRs. MDRs received between 2016 and 2022 averaged 148 ± 17 MDRs per year.

Additionally, FDA conducted a comprehensive literature review to identify and gather relevant published information regarding the safety and effectiveness of solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives. Consequently, FDA concludes there is inadequate information characterizing the safety and effectiveness of wound dressings and liquid wound washes containing medically important antimicrobials. The 510(k) clearances of these devices were based solely on nonclinical information and determinations of substantial equivalence to the preamendments device in accordance with section 513(i) of the FD&C Act, which, in light of the available information regarding the risks with no information supporting the benefit of these devices, is inadequate to support a reasonable assurance of safety and effectiveness for these devices.

FDA also reviewed recalls reported under product code FRO from 2003 to July 2022.[3] There are no recalls for solid wound dressings; wound dressings formulated as a gel, cream, or ointment; or liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives.

On September 20 and 21, 2016, FDA convened the General and Plastic Surgery Device Panel described in section II (Ref. 3). The majority of the 2016 Panel members noted that there is a lack of clinical data to demonstrate a clear clinical benefit regarding the use of wound dressings and liquid wound washes containing medically important antimicrobials. Several of the 2016 Panel members noted that wound dressings and liquid wound washes containing medically important antimicrobials, such as antibiotics, present an unreasonable risk of illness or injury to the patient (*e.g.,* directly contributing to the spread of antimicrobial resistance, further limiting clinician's therapeutic options), especially given the lack of probable benefit. Additionally, the 2016 Panel members discussed that special

[3] Only the product code FRO was queried for the recall analysis as the majority of the products in scope for this proposed order fall under FRO. The types of recalls reported under FRO are expected to be representative of all products in scope for this proposed order.

controls, such as testing in an animal model, could not be used to evaluate and/or mitigate the high level of AMR risk. As such, several panelists concluded that these wound dressings and liquid wound washes should be classified as class III and subject to increased regulatory controls to mitigate the high level of AMR risk.

B. Benefits of the Device

The purported benefit of the use of wound dressings and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives include maintaining a moist environment, providing an effective barrier to environmental contaminants, reducing microbial growth within the dressing, and extending the shelf life of non-sterile and/or multiple-use wound dressings and liquid wound washes; however, FDA is not aware of clinical evidence supporting the stated benefit of wound dressings and liquid wound washes containing medically important antimicrobials. FDA is proposing a PMA be filed to require that manufacturers demonstrate that a reasonable assurance of safety and effectiveness exists for solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives.

C. Risks to Health

The unreasonable risk profile of solid wound dressings; wound dressings formulated as a gel, cream, or ointment; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives includes adverse tissue reaction, immunological reaction, transmission of pathogens and parasites, toxicity, delayed wound healing, incompatibility with other therapies, contribution to the spread of AMR, infection, microbial growth within the product during use, product degradation during stated shelf storage, retention of dressing material in wound, loss of barrier function, inability to remove wound debris and foreign materials, and negatively impacting the skin microbiota in the peri-wound area resulting in impaired wound healing.

FDA agrees with certain 2016 Panel members that wound dressings and liquid wound washes containing medically important antimicrobials present an unreasonable risk of illness or injury. FDA further agrees that because insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness, wound dressings and liquid wound washes containing medically important antimicrobials should be class III subject to PMA.

VI. PMA Requirements

A PMA for solid wound dressings; wound dressings formulated as gels, creams, and ointments; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives must include the information required by section 515(c)(1) of the FD&C Act. Such a PMA should also include a detailed discussion of the risks identified in section V, as well as a discussion of the effectiveness of the product for which premarket approval is sought. In addition, a PMA must include all data and information on the following: (1) any risks known, or that should be reasonably known, to the applicant that have not been identified in this document; (2) the effectiveness of the device that is the subject of the application; and (3) full reports of all preclinical and clinical information from investigations on the safety and effectiveness of the device for which premarket approval is sought.

A PMA must include valid scientific evidence to demonstrate reasonable assurance of the safety and effectiveness of the solid wound dressing; wound dressing formulated as gels, creams, and ointments; or liquid wound wash containing medically important antimicrobials acting as either protectants or preservatives for its intended use (see § 860.7(c)(2) (21 CFR 860.7(c)(2))). FDA defines valid scientific evidence in § 860.7(c)(2).

To present reasonable assurance of safety and effectiveness of solid wound dressings; wound dressings formulated as gels, creams, and ointments; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives, FDA tentatively concludes that manufacturers should submit performance testing to support PMA approval. Existing published clinical literature relevant to the product may also be leveraged as part of the PMA submission. In addition, FDA strongly encourages manufacturers to meet with the Agency early through the Q-Submission Program [4] for any assistance in preparation of their PMA.

[4] See FDA guidance, ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program; Guidance for Industry and Food and Drug Administration Staff.'' June 2, 2023, available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.*

VII. Analysis of Environmental Impact

We have determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Paperwork Reduction Act of 1995

While this proposed order contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The collections of information in 21 CFR part 814, subparts A through E, have been approved under OMB control number 0910–0231; and the collections of information in part 812 have been approved under OMB control number 0910–0078.

IX. Proposed Effective Date

FDA is proposing that any final order based on this proposal become effective on the date of its publication in the **Federal Register** or at a later date if stated in the final order.

X. Opportunity To Request a Change in Classification

Before requiring the filing of a PMA or notice of completion of a PDP for a device, FDA is required by section 515(b)(2)(D) of the FD&C Act to provide an opportunity for interested persons to request a change in the classification of the device based on new information relevant to the classification of the device. A request for a change in the classification of solid wound dressings; wound dressings formulated as gels, creams, and ointments; and liquid wound washes containing medically important antimicrobials acting as either protectants or preservatives, as described in this document, should be provided in response to the proposed rule issued elsewhere in this issue of the **Federal Register** and contain the information required by 21 CFR 860.123, including new information relevant to the classification of the device.

XI. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for

viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at *https://www.regulations.gov.* References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

* 1. General and Plastic Surgery Devices Panel, ''Transcript of the FDA General and Plastic Surgery Devices Panel meeting—November 17, 1998.'' Available at *https://web.archive.org/web/20180125235924/https://www.fda.gov/ohrms/dockets/ac/98/transcpt/3483t1.pdf.*
* 2. General and Plastic Surgery Devices Panel, ''Brief Summary from the General and Plastic Surgery Devices Panel Meeting—August 25–26, 2005.'' Available at *https://wayback.archive-it.org/7993/20170405192855/https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/GeneralandPlasticSurgeryDevicesPanel/ucm124755.htm.*
* 3. General and Plastic Surgery Devices Panel, ''2016 Meeting Materials of the General and Plastic Surgery Advisory Panel—September 20–21, 2016.'' Available at *https://wayback.archive-it.org/7993/20201227032045/https://www.fda.gov/advisory-committees/general-and-plastic-surgery-devices-panel/2016-meeting-materials-general-and-plastic-surgery-advisory-panel.*
4. WHO, Critically Important Antimicrobials for Human Medicine. 2018. Available at *https://www.who.int/publications/i/item/9789241515528.*

List of Subjects in 21 CFR Part 878

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, we propose that 21 CFR part 878 be amended as follows:

PART 878—GENERAL AND PLASTIC SURGERY DEVICES

■ 1. The authority citation for part 878 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

■ 2. Amend § 878.4016, as proposed to be added in FR 2023–26209, published elsewhere in this issue of the **Federal Register**, by adding paragraph (c) to read as follows:

§ 878.4016 Solid wound dressings containing antimicrobials and/or other chemicals.

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of product development protocol (PDP) is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [DATE OF THE LAST DAY OF THE 30TH FULL CALENDAR MONTH AFTER EFFECTIVE DATE OF FINAL RULE], for any solid wound dressing, as identified in paragraph (a) of this section, that either contains one or more medically important antimicrobials acting as protectants and was in commercial distribution before May 28, 1976, or has, on or before [DATE OF THE LAST DAY OF THE 30TH FULL CALENDAR MONTH AFTER EFFECTIVE DATE OF FINAL RULE], been found to be substantially equivalent to any solid wound dressing, as identified in paragraph (a) of this section, that contains one or more medically important antimicrobials acting as protectants and that was in commercial distribution before May 28, 1976. Any other solid wound dressing, as identified in paragraph (a) of this section, that contains one or more medically important antimicrobials acting as protectants shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

■ 3. Amend § 878.4017, as proposed to be added in FR 2023–26209, published elsewhere in this issue of the **Federal Register**, by adding paragraph (c) to read as follows:

§ 878.4017 Wound dressings formulated as a gel, cream, or ointment containing antimicrobials and/or other chemicals.

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of product development protocol (PDP) is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [DATE OF THE LAST DAY OF THE 30TH FULL CALENDAR MONTH AFTER EFFECTIVE DATE OF FINAL RULE], for any wound dressing formulated as a gel, cream, or ointment, as identified in paragraph (a) of this section, that either contains one or more medically important antimicrobials acting as preservatives and was in commercial distribution before May 28, 1976, or has, on or before [A DATE OF THE LAST DAY OF THE 30TH FULL CALENDAR MONTH AFTER EFFECTIVE DATE OF FINAL RULE], been found to be substantially equivalent to any wound dressings formulated as a gel, cream, or ointment, as identified in paragraph (a) of this section, that contains one or more medically important antimicrobials acting as preservatives and that was in commercial distribution before May 28, 1976. Any other wound dressing formulated as a gel, cream, or ointment, as identified in paragraph (a) of this section, that contains one or more medically important antimicrobials acting as preservatives shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

■ 4. Amend § 878.4019, as proposed to be added in FR 2023–26209, published elsewhere in this issue of the **Federal Register**, by adding paragraph (c) to read as follows:

§ 878.4019 Liquid wound washes.

* * * * *

(c) Date premarket approval application (PMA) or notice of completion of product development protocol (PDP) is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [DATE OF THE LAST DAY OF THE 30TH FULL CALENDAR MONTH AFTER EFFECTIVE DATE OF THE FINAL RULE], for any liquid wound wash, as identified in paragraph (a) of this section, that either contains one or more medically important antimicrobials acting as preservatives and was in commercial distribution before May 28, 1976, or has, on or before [DATE OF THE LAST DAY OF THE 30TH FULL CALENDAR MONTH AFTER EFFECTIVE DATE OF THE FINAL RULE], been found to be substantially equivalent to any liquid wound wash, as identified in paragraph (a) of this section, that contains one or more medically important antimicrobials acting as preservatives and that was in commercial distribution before May 28, 1976. Any other liquid wound wash, as identified in paragraph (a) of this section, that contains one or more medically important antimicrobials acting as preservatives shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: November 22, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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