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Menstrual Products – Performance Testing and Labeling Recommendations

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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For questions about this document, contact OHT3: Office of Gastro-Renal, ObGyn, General Hospital, and Urology Devices/DHT3B: Division of Reproductive, Gynecology, and Urology Devices at (301) 796-7030.

When final, this guidance will supersede "Menstrual Tampons and Pads: Information for Premarket Notification Submissions (510(k)s)," issued on July 27, 2005.

FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Preface

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Menstrual Products – Performance Testing and Labeling Recommendations

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

This draft guidance document provides recommendations for menstrual product[1] performance testing and labeling, as well as information for inclusion in premarket notification (510(k)) submissions, when necessary, for certain menstrual products. The recommendations in this guidance apply to tampons, pads, and menstrual cups used to absorb or collect menstrual fluid or other vaginal discharge. The recommendations reflect updated best practices for the labeling and performance testing of menstrual products, as well as current review practices for menstrual products subject to premarket notification requirements. These recommendations are intended to promote consistency and transparency in product labeling and testing for manufacturers of these devices.

For the current edition of the FDA-recognized standard(s) referenced in this document, see the FDA Recognized Consensus Standards Database. If submitting a Declaration of Conformity to a recognized standard, we recommend you include the appropriate supporting documentation. For more information regarding use of consensus standards in regulatory submissions, refer to the FDA guidance titled "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices."

In general, FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a

[1] For purposes of this guidance, menstrual products refers to tampons, pads, and menstrual cups used to absorb or collect menstrual fluid or other vaginal discharge.

topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

In the fiscal year 2022 and 2023 appropriations reports from the House Appropriations Committee,[2,3] the Committee requested that FDA update its existing guidance on tampons and pads, "Menstrual Tampons and Pads: Information for Premarket Notification Submissions (510(k)s)," issued on July 27, 2005. These reports focused largely on recommendations related to menstrual product materials (e.g., disclosing ingredients and evaluating contaminants), reflecting growing public interest for increased transparency about the materials used to make tampons. In addition, FDA is aware of concerns about the potential release of metals from tampons after a 2024 study reported metals in tampons during laboratory testing.[4] However, the methods used in the 2024 study did not allow for estimation of toxicological risks associated with tampons, as there was no consideration of the amount of metals released from the tampon materials. As a result, FDA commissioned an independent, systematic literature review to evaluate the metal content in tampons sold in the United States (US) and the amount of metals which might thereafter be absorbed by users. Although limitations were identified in the systematic literature review, as is common, the findings did not identify safety concerns associated with tampon use and contaminant exposure.[5]

This draft guidance, which when final will supersede "Menstrual Tampons and Pads: Information for Premarket Notification Submissions (510(k)s)," includes information requested by the Committee in these appropriations reports and provides additional detail and clarifications to existing recommendations that are intended to enhance transparency and consistency of menstrual product labeling and performance testing. Specifically, the draft guidance includes recommendations for:

- menstrual cups;
- disclosing ingredients (including fragrances/deodorants) on all menstrual product outer package labels;
- evaluating contaminants for all menstrual products;

[2] H. Rept. 117-82 - AGRICULTURE, RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION, AND RELATED AGENCIES APPROPRIATIONS BILL, 2022. (accessed 2024, November 14). https://www.congress.gov/congressional-report/117th-congress/house-report/82/1

[3] H. Rept. 117-392 - AGRICULTURE, RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION, AND RELATED AGENCIES APPROPRIATIONS BILL, 2023. (accessed 2024, November 7). https://www.congress.gov/congressional-report/117th-congress/house-report/392/1

[4] Shearston JA, Upson K, Gordon M, et al. Tampons as a source of exposure to metal(loid)s. Environment International. 2024;190(108849):108849-108849. https://doi.org/10.1016/j.envint.2024.108849

[5] For more information, see the final report, dated December 5, 2024, "Contaminants in Vaginal Tampons: A Systematic Literature Review (SLR)."

- test methods that can be used for evaluating tampons for Toxic Shock Syndrome (TSS) risk and effect on vaginal microflora; and
- clarification of test methods for non-clinical bench testing of tampons.

This guidance document provides recommendations for devices that are subject to different statutory and regulatory requirements. For example, some of the menstrual products within the scope of the guidance are subject to premarket notification requirements whereas others are exempt from premarket notification requirements subject to the limitations in 21 CFR 884.9. The guidance also provides recommendations for certain menstrual products that are subject to specific labeling requirements (see 21 CFR 801.430). Notably, all of the devices within the scope of the guidance are subject to, among others, general device labeling requirements (see 21 CFR Part 801) and applicable quality system regulation (QSR) (21 CFR Part 820) requirements,[6] including but not limited to requirements regarding design controls (21 CFR 820.30), nonconforming products (21 CFR 820.90), and corrective and preventative action (21 CFR 820.100). The QSR also includes requirements to review and approve modifications to device design and production (21 CFR 820.30 and 820.70), and requirements to document changes and approvals in the device master record (21 CFR 820.181).

This guidance document supplements other FDA documents regarding the specific content requirements and recommendations of a 510(k) submission. Those submitting 510(k)s for menstrual products should also refer to 21 CFR 807.87 and FDA's guidance, "Electronic Submission Template for Medical Device 510(k) Submissions."

III. Scope

One of the specific requests in the 2023 appropriations report[7] was for FDA to publish updated and/or new guidance inclusive of additional categories of menstrual products. The scope of this guidance therefore includes menstrual products regulated under the following classification regulations, 21 CFR 884.5425, 884.5435, 884.5460, 884.5470, and 884.5400, with product codes identified in Table 1.[8] Some of these menstrual products are regulated under classification

[6] On February 2, 2024, FDA issued a final rule amending the device quality system (QS) regulation, 21 CFR Part 820, to align more closely with international consensus standards for devices. FDA also made conforming amendments to 21 CFR Part 4 (89 FR 7496). This final rule will take effect on February 2, 2026. Once in effect, this rule will amend the majority of the current requirements in Part 820 and incorporate by reference the 2016 edition of the International Organization for Standardization (ISO) 13485, Medical devices – Quality management systems – Requirements for regulatory purposes, in Part 820. As stated in the final rule, the requirements in ISO 13485 are, when taken in totality, substantially similar to the requirements of the current Part 820, providing a similar level of assurance in a firm's quality management system and ability to consistently manufacture devices that are safe and effective and otherwise in compliance with the FD&C Act. When the final rule takes effect, FDA will also update the references to provisions in 21 CFR Part 820 in this guidance to be consistent with that final rule.

[7] H. Rept. 117-392 - AGRICULTURE, RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION, AND RELATED AGENCIES APPRO- PRIATIONS BILL, 2023. (accessed 2024, November 7). https://www.congress.gov/congressional-report/117th-congress/house-report/392/1

[8] Maternity kits that include unscented menstrual pads (regulated under 21 CFR 884.5435 under product code PVT) are considered convenience kits, which are outside the scope of this guidance. See "Convenience Kits Interim Regulatory Guidance," for more information.

regulations that have additional requirements (i.e., 21 CFR 884.5460 and 884.5470 are subject to the labeling requirements in 21 CFR 801.430) or that are exempt from premarket notification requirements.[9] To help identify which recommendations and/or requirements are applicable for each type of menstrual product, Table 1 lists the specific sections of this guidance document that are relevant for each product code.[10]

Table 1. Device Types within the Scope of This Guidance.

Product Code	Device Class & 510(k) Requirements	Product Code Name	Regulation Number	Description	Relevant Guidance Sections
HHL	Class 2; 510(k) Exempt	Pad, Menstrual, Scented, Scented-Deodorized	21 CFR 884.5425	Scented or scented-deodorized menstrual pads used to absorb menstrual or other vaginal discharge, including those intended as intralabial pads or reusable menstrual pads. These are made with materials that do not meet the requirements for Class 1 per 21 CFR 884.5425(b).	V VI.B(1), (3) VII.B

[9] Products identified as 'exempt' in Table 1 are exempt from the requirement to submit a premarket notification (510(k)) unless the product exceeds the limitations of the exemption from premarket notification identified in 21 CFR 884.9.

[10] FDA's Center for Devices and Radiological Health (CDRH) uses product codes to help categorize and assure consistent regulation of medical devices. A product code consists of three characters that are assigned at the time a product code is generated and is unique to a product type. The three characters carry no other significance and are not an abbreviation.

Product Code	Device Class & 510(k) Requirements	Product Code Name	Regulation Number	Description	Relevant Guidance Sections
NRC	Class 1; 510(k) Exempt	Pad, Menstrual, Scented, Scented-Deodorized Made of Common Cellulosic And Synthetic Material With An Established Safety Profile	21 CFR 884.5425	Scented or scented-deodorized menstrual pads used to absorb menstrual or other vaginal discharge, not intended as intralabial pads or reusable menstrual pads. These are made of common cellulosic or synthetic material with an established safety profile.	V VI.B(1), (3) VII.B
NUR	Class 1; 510(k) Exempt	Pad, Menstrual, Intralabial[11]	21 CFR 884.5435	An unscented menstrual pad intended as an intralabial pad, which is placed over the vaginal introitus to absorb menstrual fluid or other vaginal discharge and is made of common cellulosic or synthetic material with an established safety profile.	V VI.B(1), (3) VII.B

[11] An intralabial pad is a menstrual pad intended to be worn externally and held in place by the labia.

Product Code	Device Class & 510(k) Requirements	Product Code Name	Regulation Number	Description	Relevant Guidance Sections
NUQ[12]	Class 1; 510(k) Exempt	Pad, Menstrual, Reusable[13]	21 CFR 884.5435	A reusable, unscented menstrual pad which is used to absorb menstrual fluid or other vaginal discharge and is made of common cellulosic or synthetic material with an established safety profile.	V VI.B(1), (3) VII.B
HHD	Class 1; 510(k) Exempt	Pad, Menstrual, Unscented	21 CFR 884.5435	An unscented menstrual pad which is used to absorb menstrual fluid or other vaginal discharge and is made of common cellulosic and synthetic material with an established safety profile.	V VI.B(1), (3) VII.B
HIL	Class 2; 510(k)	Tampon, Menstrual, Scented, Scented-Deodorized	21 CFR 884.5460	A scented or scented-deodorized menstrual tampon is a plug made of cellulosic or synthetic material that is inserted into the vagina and used to absorb menstrual fluid or other vaginal discharge.	IV V VI.A VII.A VIII

[12] Period underwear are regulated under 21 CFR 884.5435, under product code NUQ.
[13] A reusable pad is one that may be washed, dried, and used again by the same woman.

Product Code	Device Class & 510(k) Requirements	Product Code Name	Regulation Number	Description	Relevant Guidance Sections
HEB	Class 2; 510(k)	Tampon, Menstrual, Unscented	21 CFR 884.5470	An unscented menstrual tampon is a plug made of cellulosic or synthetic material that is inserted into the vagina and used to absorb menstrual fluid or other vaginal discharge.	IV V VI.A VII.A VIII
HHE	Class 2; 510(k) Exempt	Menstrual Cup	21 CFR 884.5400	A menstrual cup is a receptacle placed in the vagina to collect menstrual flow.	V VI.B VII.B

When determining whether to submit a premarket notification for these devices, you should assess whether your device has the same intended use as legally marketed devices of that generic type and whether your device has the same technological characteristics as legally marketed devices within that generic type (see 21 CFR 884.9 for the limitations of the exemption from premarket notification).

Generally, FDA believes a material has an established safety profile if it has a history of safe use for similar intended uses and is physically and chemically well-characterized. The characterization of the material may be in the published literature, a previous submission, or a Device Master File (MAF).[14]

If your menstrual product contains a drug or biological product, it is a combination product. Menstrual product combination products are not exempt from marketing submissions and may have different regulatory pathways. See FDA's Office of Combination Products webpage for more information.

IV. Predicate Comparison (Devices subject to 510(k) requirements)

For devices subject to 510(k) requirements, manufacturers compare their new device to a similar legally marketed predicate device and must demonstrate substantial equivalence to that predicate

[14] For information about MAFs, see 21 CFR 814.3(d) and FDA's Device Master Files webpage.

(section 513(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); 21 CFR 807.87(f)). This comparison in the 510(k) should show how your device is similar to and different from the predicate. Side by side comparisons, whenever possible, are desirable. See Table 2 for an example of how this information may be organized. This table is not intended to represent an exhaustive list of comparative parameters; we recommend you provide all relevant device descriptive characteristics as outlined in the "Device Description" section V.A.

Table 2. Sample predicate device comparison table to outline differences and similarities between the subject and predicate devices.

Description	Subject Device	Predicate Device (Kxxxxxx)
Device Name		
Classification Regulation		
Product Code		
Intended Use		
Design (e.g., configuration of the tampon and applicator, if present)		
Applicator (yes/no)		
Dimensions		
Absorbency range(s) (grams) (tampons only)		
Component Materials (chemical composition)		
Additives and Finishing Agents		
Sterile (yes/no)		
Single use/reprocessed		
Other Features (if any)		

V. Device Description in the 510(k) or Device Master Record

For devices subject to 510(k) requirements, you should identify, in your 510(k) submission, your device by the applicable classification regulation number and product code, as indicated in Section III, and include the information described within this section. We also recommend that you provide a complete discussion of the design features, indications, and performance characteristics of your device.[15] You should also discuss the similarities and differences between your device and the predicate device, as indicated in Section IV, in sufficient detail to permit FDA to fully assess your device and compare it with the predicate device. We also recommend that you describe how any differences in indications for use or technological characteristics may affect the safety or effectiveness of your device. For devices that are exempt from 510(k)

[15] 21 CFR 807.92.

requirements, we recommend that you identify, in your device master record, your device by the applicable classification regulation number and product code, as indicated in Section III, and refer to the classification regulation and product code to determine which regulations and requirements apply to your device. For all menstrual products, we recommend that you include the following in your 510(k) submission (if the device is subject to 510(k) requirements) or in your device master record (if the device is exempt from 510(k) requirements).

A. Design and Dimensions

Tampons

FDA recommends that you include engineering drawings of the tampon. We also recommend that you identify the dimensions and materials for the:

- pledget
- overwrap (cover)
- removal string
- applicator (if any).

FDA also recommends that you provide a cross-sectional drawing to illustrate the design and dimensions of the pre-absorption tampon, both compressed and uncompressed.

Pads

FDA recommends that you include engineering drawings of the pad. We also recommend that you show the dimensions and materials for the:

- core
- overwrap (cover).

Menstrual cups

FDA recommends that you include information on the material, dimensions, and volume of the reusable cup in addition to a description of any coatings and applicators. We also recommend that you describe how to appropriately insert the menstrual cup and include any additional information about the applicator component, if used during the insertion process.

B. Absorbency Range

Tampons

Ranges of absorbency for tampons (in grams) are identified in 21 CFR 801.430 (e)(1). To support the required labeling for tampons, FDA recommends that you provide specifications, including tolerances for the weight of the pledget (in grams), for each absorbency range of tampon in your submission. We also

recommend that you identify the absorbency ranges for each tampon included in your 510(k) submission.

Pads

Absorbency range as described in 21 CFR 801.430 does not apply to pads. See Design and Dimensions above instead.

Menstrual Cups

Absorbency range does not apply to menstrual cups, which do not absorb fluid. However, FDA recommends that you provide specifications for the volume of menstrual fluid that the menstrual cup can hold for the stated duration of use.

C. Component Materials (including Additives)

For all component materials present in a tampon, applicator, pad, or menstrual cup, we recommend that you identify:

- detailed chemical identity and quantity (in µg per tampon or pad) for all components, and any additives or finishing (e.g., anti-wicking) agents.
- chemical identity of each component of any fragrance, deodorants or pigments.
- letter of authorization (LOA) to reference relevant MAFs for component materials, whenever possible.

VI. Performance Testing Recommendations

Pursuant to section 502(f) of the FD&C Act and 21 CFR 801.5, a device must have labeling that bears adequate directions for use, meaning directions under which the layman can use a device safely and for the purposes for which it is intended. Due to the nature and duration of contact of menstrual products, in order for the device to be used safely when used as intended, we recommend the performance testing discussed in this section to evaluate the safety of the materials and performance characteristics of the device. Such testing will help to inform what is needed to ensure, among other things, the adequacy of the directions for use included in the labeling. Such recommended performance testing, and documentation of such testing, will also help to ensure compliance with the QSR (21 CFR Part 820) and record requirements to the extent required under applicable law, including in the QSR (e.g., 21 CFR 820.30(j)). Notably, QSR records and other records required under the FD&C Act must generally be made available to an FDA investigator upon request (see section 704(e) of the FD&C Act).

A. Tampons

In addition to helping a manufacturer comply with the labeling and QSR requirements discussed above, the recommendations in this section may help a manufacturer to establish substantial equivalence to a legally marketed predicate device as performance data is typically needed to do so.[16]

(1) Biocompatibility

Significance: Tampons contain patient-contacting materials, which, when used for their intended purpose, (i.e., contact type and duration), may induce a harmful biological response.

Recommendation: You should determine the biocompatibility of all patient-contacting component materials present in your tampon. If your tampon is identical in chemical composition, manufacturing and processing methods to a tampon of the same type with a history of safe use, you may reference previous testing experience or the literature, if appropriate. For some device materials, it may be appropriate to provide a reference to either a recognized consensus standard, or to an LOA for a MAF. You should refer to the FDA's Device Master Files webpage for additional information on using MAFs.

If you are unable to identify a legally marketed device with the same nature of contact and contact duration that uses the same materials, manufacturing and processing methods as used in your device, we recommend you conduct and provide a biocompatibility evaluation as recommended in FDA's guidance "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process.'" The evaluation should explain the relationship between the identified biocompatibility risks, the information available to mitigate the identified risks, and knowledge gaps that remain. You should then identify any biocompatibility testing or other evaluations that were conducted to mitigate any remaining risks. We recommend that you consider the recommendations in this guidance, which identifies the types of biocompatibility assessments that should be considered and recommendations regarding how to conduct related tests.

As described in ISO 10993-1 *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* and Attachment A of FDA's guidance on ISO 10993-1, menstrual products are surface devices in contact with mucosal membrane for a long term contact duration. Although each individual use is of limited (i.e., <24 hour) duration, the overall lifetime use of tampons can lead to a cumulative exposure exceeding >30 days with repeat use. Therefore, the following endpoints should be addressed in your biocompatibility evaluation:

- Cytotoxicity per ISO 10993-5 *Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity*, using a direct contact method;

[16] The information required in a premarket notification submission is identified in 21 CFR 807.07. See 21 CFR 807.100(b) for the criteria FDA uses to determine that a device is substantially equivalent.

- Sensitization per ISO 10993-10 *Biological evaluation of medical devices – Part 10: Tests for skin sensitization*, (e.g., Guinea Pig Maximization Test)[17];
- Irritation per ISO 10993-23 *Biological evaluation of medical devices – Part 23: Tests for irritation*, (e.g., Vaginal Irritation);
- Acute Systemic Toxicity per ISO 10993-11 *Biological evaluation of medical devices – Part 11: Tests for systemic toxicity*;
- Material-mediated Pyrogenicity per USP 34 *Rabbit Pyrogen Test*;
- Subacute/subchronic Toxicity;
- Genotoxicity;
- Implantation per ISO 10993-6 *Biological evaluation of medical devices – Part 6: Tests for local effects after implantation*;
- Chronic Toxicity

Some test methods for the above endpoints are part of the Accreditation Scheme for Conformity Assessment (ASCA) Program, which may be leveraged by manufacturers to enhance efficiency of the premarket review process by increasing FDA's confidence in these test results. For more information, see the ASCA Program website.

If the tampon is made of materials with well-established safety profiles consistent with previously cleared devices (e.g., cotton), a subset of the above testing may be sufficient to demonstrate biocompatibility. You should identify a listing of the component materials of the device (including any additives), as well as include a discussion of why the materials' safety is well-established. This should include if the material has had previous use in devices of the same type (e.g., in the predicate or other FDA-cleared devices). The following abbreviated list of biocompatibility endpoints should be evaluated for all tampons (following the same methods identified above):

- Cytotoxicity
- Sensitization
- Irritation
- Acute Systemic Toxicity

The following additional considerations are recommended for tampons:

- In addition to the above, devices made with cotton or other naturally sourced fiber should be evaluated for the presence of contaminants, such as chemical residues.

[17] FDA supports the principles of the "3Rs" to replace, reduce, and/or refine animal use in testing, when feasible. We encourage manufacturers to consult with FDA if they wish to use a non-animal testing method that they believe is suitable, adequate, validated, and feasible. We will consider if a proposed alternative method could be assessed for equivalency to an animal test method.

- FDA recommends that devices made with naturally sourced materials not contain 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD)/2,3,7,8-tetrachlorofuran dioxin (TCDF) and any pesticide and herbicide residues.[18]

- You should describe any assurances that contaminants are not present or, if contaminants are present, the level present and the method used to assess it. These assurances may include, but are not limited to, test methods, tolerances, or acceptance criteria. We recommend you conduct a risk analysis considering the materials, sources, and processing of device component materials to identify any potential contaminants accordingly.[19]

- For any materials bleached during processing, we recommend that you identify the bleaching process used, e.g., Elemental Chlorine-Free (ECF) or Totally Chlorine-Free (TCF).

- If a device contains novel materials (e.g., a device made from a new type of fiber) or materials with known biocompatibility risk, the abbreviated list of biocompatibility testing may not be sufficient to support biocompatibility of the device.

- If the tampon has an applicator, the applicator should be tested separately. Because applicators have transient usage, biocompatibility evaluation consistent with limited mucosal contact duration in accordance with ISO 10993-1: *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* and Attachment A of FDA's guidance on ISO-10993-1 is appropriate (i.e., cytotoxicity, irritation, and sensitization).

(2) Microbiology Assessment

Significance: Due to the nature and duration of contact in the vagina, indwelling menstrual products may induce a potentially life-threatening condition, TSS. Therefore, tampons should be assessed to determine if they enhance the growth of the bacteria that causes TSS. The recommendations identified in this section are anticipated to address potential risks related to vaginal infection and TSS for tampons.

Recommendation: For tampons, we recommend testing that can help you demonstrate the tampon, in its final manufactured form, does not:

[18] FDA recommends that as a part of your design validation, you have in place validated test plans for monitoring dioxin and potential pesticide residues for cotton in device materials and final finished devices. We recommend that you evaluate your tampon as described in your test plans and identify the test method and name and address of the testing laboratory in your design history file. You should also explain in your design history file whether testing was conducted on a prototype, on select or all batches, and on a fixed or "as needed" schedule. For more information on design validation and design history files, please see 21 CFR Part 820 Quality Systems, Design Controls (21 CFR 820.30(i)) and Design History File (21 CFR 820.30(j)).

[19] ANSI/AAMI/ISO 14971 *Medical devices—Application of risk management to medical devices*

- enhance the growth of *Staphylococcus aureus (S. aureus)*
- increase the production of Toxic Shock Syndrome Toxin-1 (TSST-1)
- alter the growth of normal vaginal microflora.

For TSS testing of tampons, we recommend that you specify the test conditions, including cell culture medium and strains of *S. aureus* and other microorganisms used, and reference the methodology.

There are currently no recognized consensus standards to assess the tampon's potential in promoting the production of TSST-1 by *S. aureus* and its impact in the growth of normal vaginal microflora. Hence, we have included several methods that can be used for testing tampons, which are derived from published literature and FDA's experience evaluating such studies as part of marketing submissions.

a. TSST-1 Testing

For each test, you should use a clinically relevant strain of *S. aureus* (e.g., *S. aureus* MN8) that produces menstrual TSST-1. Tests should use a minimum of five replicates for each test and control samples. The test methods currently included in this guidance use specific procedures and analytical tools, such as enzyme-linked immunosorbent assay (ELISA), to identify quantifiable amounts of TSST-1 toxin present in samples tested. Any of the following test methods are recommended:

- Method 1 – Tampon Sac (adapted from Reiser *et al*., 1987,[20] Schlievert PM and Davis CC 2020,[21] Nonfoux L *et al*., 2018,[22] and Schlievert PM, 1995[23])
    - Pre-weighed tampons (test sample) should be inserted into sterile dialysis sacs inoculated with the TSST-1 producing *S. aureus* strain (concentration > 10^6 colony-forming units (CFU)/mL). The sacs should be submerged into Brain Heart Infusion (BHI) agar, incubated at 37°C for 18 hours. The tampons are then removed, weighed and extracted.
    - Adequate controls should be used to demonstrate adequate testing conditions (e.g., inoculated sac only submerged in BHI agar, an inert material into an empty applicator (all sterile)).

[20] Reiser RF, Hinzman SJ, Bergdoll MS. Production of toxic shock syndrome toxin 1 by *Staphylococcus aureus* restricted to endogenous air in tampons. J Clin Microbiol. 1987 Aug; 25(8):1450-2. https://doi.org/10.1128/jcm.25.8.1450-1452.1987

[21] Schlievert PM, Davis CC. Device-Associated Menstrual Toxic Shock Syndrome. Clin Microbiol Rev 2020; 33:3. https://doi.org/10.1128/cmr.00032-19

[22] Nonfoux L, Chiaruzzi M, Badiou C, Baude J, Tristan A, Thioulouse J, Muller D, Prigent-Combaret C, Lina G. Impact of Currently Marketed Tampons and Menstrual Cups on *Staphylococcus aureus* Growth and Toxic Shock Syndrome Toxin 1 Production In Vitro. Appl Environ Microbiol 2018; 84:12. https://doi.org/10.1128/AEM.00351-18

[23] Schlivert PM. Comparison of cotton and cotton/rayon tampon for effect on production of toxic shock syndrome toxin. J Infect Dis 1995;172:112-4. https://doi.org/10.1093/infdis/172.4.1112

- Use of a predicate device for comparison could be considered. The results from your testing should be adequately justified.
- Microbial enumeration data and TSST-1 quantification (e.g., by ELISA) can help demonstrate no increase in *S. aureus* and toxin production in the test sample as compared to the negative control.

- Method 2 - Syringe Method (adapted from Lee *et al.,* 1987,[24] and Wong and Downs, 1989[25])
  - 25-30 mL syringes should be used to simulate the dimensions of the vaginal vault.[26] Tampons (test sample) are placed within the syringes without the syringe plunger and the entire set-up is sterilized (e.g., by autoclaving).
  - BHI broth containing artificial blood should be inoculated with a minimum concentration of $1x10^6$ CFU/mL *S. aureus*. This suspension (mL per gram of test sample) is added to each syringe containing a test sample. The syringes should be sealed by placing a sterilized septa inside them to include only the air volume from the test sample and incubated at 37°C for 24 hours.
  - Culture fluids should be expressed by inserting the syringe plunger and forcing it down on the inoculated test sample. The expressed culture fluid should be used to enumerate bacterial count (plating) and quantify toxin produced (e.g., by double antibody sandwich ELISA).
  - Use of a predicate device for comparison could be considered. The results from your testing should be adequately justified.
  - Adequate positive and negative control data should be correlated to demonstrate no increase in *S. aureus* and toxin production in the test sample.

- Method 3 – Shake Flask Method (adapted from Schlievert and Blomster, 1983,[27] Schlievert PM 2020,[28] Sica VP *et al*., 2022,[29] Parsonnet *et al.*, 1996[30])

[24] Lee AC, Crass BA, Bergdoll MS. Investigation by syringe method of effect of tampons on production in vitro of toxic shock syndrome toxin 1 by *Staphylococcus aureus*. J Clin Microbiol. 1987 Jan; 25(1):87-90. https://doi.org/10.1128/jcm.25.1.87-90.1987

[25] Lee Wong AC and Downs SA. Investigation by improved syringe method of effects of tampon on production of toxic shock syndrome toxin-1 by *Staphylococcus aureus*. J. Cln. Microb. 1989; 2482-87. https://doi.org/10.1128/jcm.27.11.2482-2487.1989

[26] The vaginal vault is the expanded region of the vaginal canal at the internal end of the vagina.

[27] Schlievert PM, Blomster DA. Production of staphylococcal pyrogenic exotoxin type C: influence of physical and chemical factors. J Infect Dis 1983; 147:236-42. https://doi.org/10.1093/infdis/147.2.236

[28] Schlievert PM. Effect of non-absorbent intravaginal menstrual/contraceptive products on *Staphylococcus aureus* and production of the superantigen TSST-1. Eur J Clin Microbiol Infect Dis 2020; 39:31–38. https://doi.org/10.1007/s10096-019-03685-x

[29] Sica VP, Friberg MA, Teufel AG, Streicher-Scott JL, Hu p, Sauer UG, Krivos KL, Price JM, Baker TR, Abbinante-Nissen JM, and Woeller KE. Safety assessment scheme for menstrual cups and application for the evaluation of a menstrual cup comprised of medical grade silicone. Lancet 2022;86. https://doi.org/10.1016/j.ebiom.2022.104339

[30] Parsonnet J, Modern PA, Giacobbe KD. Effect of tampon composition on production of toxic shock syndrome toxin-1 by *Staphylococcus aureus* in vitro. J Infect Dis 1996; 173:98-103. https://doi.org/10.1093/infdis/173.1.98

- A minimum of $1x10^6$ CFU/mL of *S. aureus* is inoculated in a flask containing growth media (e.g., BHI broth) and tampons (test sample). The flasks are incubated at 37°C for 24 hours. A no-tampon flask with media only and a no-tampon flask with media inoculated with *S. aureus* should be evaluated as controls.
- Use of a predicate device for comparison could be considered. The results from your testing should be adequately justified.
- Bacterial enumeration is conducted by plate count. Quantitation of toxin is done by toxin-antibody methods (e.g., double-diffusion gel assay, ELISA, Western immunoblot).

Any alternate method used for TSST-1 testing should be adequately validated to demonstrate the tampon does not increase the production of TSST-1.

b. *In vitro* Vaginal Microflora Testing

To assess the effect of the subject device on normal vaginal microflora, you should use a consortium of microbes consisting of *Lactobacillus acidophilus*, *Staphylococcus aureus, Gardnerella vaginalis, Escherichia coli, Pseudomonas aeruginosa,* and *Candida albicans,* inoculated in synthetic vaginal medium to simulate the normal vaginal microflora environment.[31, 32, 33] The following considerations should be addressed with this testing:

- Ensure the final concentration of each individual organism is greater than 10^6 CFU/mL in the test flask consisting of approximately 200-250 mL of vaginal fluid medium.
- The subject device (pledgets only) should be incubated in the consortia test organisms suspension and exposed for 8 hours at 36±1°C, followed by extraction.
- The positive control should be a pledget infused with antibiotics while the negative control should be a flask with inoculated vaginal medium only (no tampon).
- A minimum number of five (5) replicates should be used for each subject and control device; including an additional predicate device for testing could be considered.
- The test organisms should be enumerated from each test flask at sampling time points, 0 hour, 6 hours, 8 hours and 24 hours.
- Each test consortia microorganism should be cultured at their respective optimal conditions and selective growth medium (e.g., De Man–Rogosa–Sharpe (MRS) agar for *Lactobacillus sp*., Modified Sabouraud Dextrose agar for *Candida sp*.).

[31] Chen X, Lu Y, Chen T, Li R. The Female Vaginal Microbiome in Health and Bacterial Vaginosis. Frontiers in Cellular and Infection Microbiology. 2021;11(631972). https://doi.org/10.3389/fcimb.2021.631972

[32] Lamont R, Sobel J, Akins R, et al. The vaginal microbiome: new information about genital tract flora using molecular based techniques. BJOG: An International Journal of Obstetrics & Gynaecology. 2011;118(5):533-549. https://doi.org/10.1111/j.1471-0528.2010.02840.x

[33] Guinan ME. Vaginal Colonization with *Staphylococcus aureus* in Healthy Women. Annals of Internal Medicine. 1982;96(6_Part_2):944. https://doi.org/10.7326/0003-4819-96-6-944

- Test reports depicting the viability (CFU/mL vs. sampling time points) of the microbial consortia (for each specific microorganism separately) in the presence of the subject device as compared to the controls should be provided.
- The test report should demonstrate all media sterility and growth controls were met. All members of the consortia in the positive control should demonstrate significant decrease (minimum of 2 log decrease) as compared to the negative control at 24 hours.
- An observed concentration difference of ≤ 1 Log is considered not significant for the subject device replicate as compared to the negative control after 24 hours.
- The acceptance criteria should be adequately specified to demonstrate that the microbial viability of each consortia organism is similar to that observed with the no tampon control.
- The results should be summarized to demonstrate that the subject device does not contribute to meaningful changes in the growth of normal vaginal flora.

For specific device types that should conduct a clinical study (see Section G for examples), vaginal microflora testing may be included as an endpoint in the clinical study to demonstrate no significant change (as compared to baseline) in the assessed flora when using the device.

(3) Non-Clinical Bench Testing

Non-clinical bench testing may be needed, among other things, to comply with the labeling requirements at 21 CFR 801.430 and to demonstrate substantial equivalence, namely that the tampon is as safe and effective as the predicate device under section 513(i)(1)(A)(ii). To assist in determining the appropriate non-clinical bench testing for your device, you can seek input from the Agency via the Q-Submission Program.[34] For information on the recommended content and format of test reports for the testing described in this section, refer to FDA's guidance, "Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions."

a. Absorbency Range

Significance: Standardization of absorbency is important to ensure users can select the appropriate size tampon for their needs. Using the lowest absorbency tampon that is effective for the individual's menstrual flow is important to reduce the risk of vaginal infection and TSS. Testing to determine the absorbency for each labeled absorbency provides an assurance of efficacy.

Recommendation: Tampons must be labeled for absorbency in accordance with 21 CFR 801.430(e). To determine the absorbency of tampons, you must use the "Syngyna testing" method as specified in 21 CFR 801.430(f)(2). You should provide a summary of this testing in your submission for each absorbency level of the tampons you intend to market.

[34] For details on the Q-Submission Program, refer to the guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program."

b. Mechanical Integrity for Tampons

Significance: Tampons are generally subjected to tensile force and sheer stress during use. Failure to withstand these forces may result in user harm (e.g., vaginal injury, prolonged exposure to device materials, infection) during tampon insertion, wear, and removal. An evaluation of string strength, fiber shedding, and tampon integrity provides assurance that the tampon can maintain its mechanical integrity throughout its duration of use.

Recommendation: FDA recommends that you demonstrate the performance characteristics for the following features of tampons:

- string strength
- fiber shedding
- tampon integrity

Fiber shedding testing should represent a worst-case use duration (at least 8 hours) of the tampon. The testing should take into account expected sheer stress from insertion and removal of the tampon from the vagina, as would occur in clinical use. The specific conditions of the test should be justified based upon typical clinical usage of the device.

(4) Clinical Performance Testing

Significance: In some limited cases, non-clinical performance testing or evaluation may not fully characterize the user experience, outcomes, and risks. In such cases, we recommend that you conduct *in vivo* (i.e., clinical) studies to evaluate device safety and effectiveness.

Recommendation: In general, clinical evidence is typically not necessary to support a determination of substantial equivalence. Clinical evidence may be requested in situations such as the following:

- indications for use dissimilar from legally marketed devices of the same type;
- new technology, i.e., technology, such as design or material formulation, different from that used in legally marketed devices of the same type, yet does not raise different questions of safety or effectiveness; cases where non-clinical performance testing or evaluation (e.g., microbiology testing) raise issues that warrant further evaluation with clinical evidence.

We encourage you to engage with the review division through the Q-Submission Program to obtain early feedback on your approach and study design. For additional information regarding the Q-Submission Program, refer to FDA guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program." We recommend that you submit a Pre-Submission (a type of Q-Submission) if you have specific questions on aspects of your study design.

If clinical studies are necessary to demonstrate that the device is as safe and effective as the predicate, for example, we recommend that the studies evaluate:

- irritation;
- allergy;
- effects on vaginal microflora;
- abrasions;
- ulceration;
- laceration; and
- residual fiber retention.

For "ultra" absorbency tampons (i.e., 15-18 grams determined by Syngyna testing, as defined in 21 CFR 801.430(f)(2)), you should provide clinical information on fiber sloughing *in vivo*, in addition to the information from the evaluations listed above. If you have already begun marketing your "ultra" absorbency tampon in another country, we recommend that you include any published literature related to the use of your "ultra" absorbency tampon, in particular any literature related to that tampon and TSS.

If subjects undergo a colposcopic examination during your clinical study to assess vaginal mucosa integrity, redness, and irritation or residual fiber retention related to tampon use, we recommend these examinations be conducted before and after the menses. We also recommend that these examinations be conducted by a health care provider. When conducting colposcopic examinations, we recommend referring to the Manual for the Standardization of Colposcopy for the Evaluation of Vaginal Products, Update 2004.[35]

Alternatives to clinical testing should be supported by an adequate scientific rationale. If a clinical investigation is conducted to determine the safety or effectiveness of a device, in support of a 510(k) submission, such investigation is subject to the Investigational Device Exemptions (IDE) regulation, 21 CFR Part 812. Generally, we believe menstrual products addressed by this guidance document would be considered non-significant risk devices; therefore, the study would likely be subject to the abbreviated requirements of 21 CFR 812.2(b). See the FDA guidance titled, "Significant Risk and Nonsignificant Risk Medical Device Studies." In addition, sponsors of clinical investigations that support 510(k) submissions are subject to FDA regulations governing institutional review boards (21 CFR Part 56) and the protection of human subjects (21 CFR Part 50), including requirements for informed consent (21 CFR Part 50, subpart B).

When data from clinical investigations conducted outside the US are submitted to FDA for these devices, the requirements of 21 CFR 812.28 may apply.[36] 21 CFR 812.28(a) outlines the conditions for FDA acceptance of data from clinical investigations conducted outside the US to support an IDE or a premarket submission. For more information, see the FDA guidance "Acceptance of Clinical Data to Support Medical Device Applications and Submissions: Frequently Asked Questions."

[35] World Health Organization. Manual for the Standardization of Colposcopy for the Evaluation of Vaginal Products, Update 2004, WHO.

[36] 21 CFR 812.28 applies to relevant clinical investigations that enroll the first subject on or after February 21, 2019, and that support an IDE or device marketing application or submission to FDA.

In some cases, "real-world data" (RWD) may be used, for example, to support changes (e.g., expansion of the indication) for a device for which 510(k) clearance has already been obtained. FDA encourages manufacturers to engage with the Agency if they have questions on RWD.[37] For additional information regarding this topic, refer to the FDA Guidance entitled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices."

B. Pads and Menstrual Cups

The following performance testing recommendations may help a manufacturer to comply with the labeling and applicable QSR requirements discussed earlier in this section.

(1) Biocompatibility

Significance: Pads and menstrual cups contain patient-contacting materials, which, when used for their intended purpose, (i.e., contact type and duration), may induce a harmful biological response.

Recommendation: You should determine the biocompatibility of all patient-contacting component materials present in your device. If your pad or menstrual cup is identical in chemical composition, manufacturing and processing methods to a menstrual product of the same type with a history of safe use, you may reference previous testing experience or the literature, if appropriate. For some device materials, it may be appropriate to provide a reference to either a recognized consensus standard, or to an LOA for a MAF. You should refer to the FDA's Device Master Files webpage for additional information on using MAFs.

If you are unable to identify a legally marketed device with the same nature of contact and contact duration that uses the same materials, manufacturing and processing methods as used in your device, we recommend you conduct a biocompatibility evaluation as recommended in FDA's guidance "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process.'" The evaluation should explain the relationship between the identified biocompatibility risks, the information available to mitigate the identified risks, and knowledge gaps that remain. You should then identify any biocompatibility testing or other evaluations that were conducted to mitigate any remaining risks. We recommend that you consider the recommendations in this guidance, which identifies the types of biocompatibility assessments that should be considered and recommendations regarding how to conduct related tests.

As described in ISO 10993-1 *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* and Attachment A of FDA's guidance on ISO 10993-1, menstrual products are surface devices in contact with mucosal membrane for a long term contact duration. Although each individual use is of limited (i.e., <24 hour) duration, the overall

[37] Manufacturers can seek input from the Agency via the Q-Submission Program. See FDA guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program."

lifetime use of pads and menstrual cups can lead to a cumulative exposure exceeding >30 days with repeat use. Therefore, the following endpoints should be addressed in your biocompatibility evaluation:

- Cytotoxicity per ISO 10993-5 *Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity*, using a direct contact method;
- Sensitization per ISO 10993-10 *Biological evaluation of medical devices – Part 10: Tests for skin sensitization*, (e.g., Guinea Pig Maximization Test);
- Irritation per ISO 10993-23 *Biological evaluation of medical devices – Part 23: Tests for irritation*, (e.g., Vaginal Irritation);
- Acute Systemic Toxicity per ISO 10993-11 *Biological evaluation of medical devices – Part 11: Tests for systemic toxicity*;
- Material-mediated Pyrogenicity per USP 34 *Rabbit Pyrogen Test*;
- Subacute/subchronic Toxicity;
- Genotoxicity;
- Implantation per ISO 10993-6 *Biological evaluation of medical devices – Part 6: Tests for local effects after implantation*;
- Chronic Toxicity

If the pad or menstrual cup is made of materials with well-established safety profiles consistent with previously cleared or marketed devices (e.g., cotton for pads, silicone for menstrual cups), a subset of the above testing may be sufficient to demonstrate biocompatibility. You should identify a listing of the component materials of the device (including any additives), as well as include a discussion of why the materials' safety is well-established. This should include if the material has had previous use in devices of the same type. The following abbreviated list of biocompatibility endpoints should be evaluated for all pads and menstrual cups (following the same methods identified above):

- Cytotoxicity
- Sensitization
- Irritation
- Acute Systemic Toxicity

The following additional considerations are recommended for pads and menstrual cups:

- In addition to the above, pads and menstrual cups made with cotton or other naturally sourced fiber should be evaluated for the presence of contaminants, such as chemical residues.

- FDA recommends that devices made with naturally sourced materials not contain 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)/2,3,7,8-tetrachlorofuran dioxin (TCDF) and any pesticide and herbicide residues.[38]

- You should describe any assurances that contaminants are not present or, if contaminants are present, the level present and the method used to assess it. These assurances may include, but are not limited to, test methods, tolerances, or acceptance criteria. We recommend you conduct a risk analysis considering the materials, sources, and processing of device component materials to identify any potential contaminants accordingly.[39]

- For any materials bleached during processing for pads, we recommend that you identify the bleaching process used, e.g., Elemental Chlorine-Free (ECF) or Totally Chlorine-Free (TCF).

- If a pad or menstrual cup contains novel materials or materials with known biocompatibility risk, the abbreviated list of biocompatibility testing may not be sufficient to support biocompatibility of the device.

- If the menstrual cup has an applicator, the applicator should be tested separately. Because applicators have transient usage, biocompatibility evaluation consistent with limited mucosal contact duration in accordance with ISO 10993-1: *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* and Attachment A of FDA's guidance on ISO-10993-1 is appropriate (i.e., cytotoxicity, irritation, and sensitization).

(2) Microbiology Assessment

Significance: Due to the nature and duration of contact in the vagina, indwelling menstrual products may induce a potentially life-threatening condition, TSS. Therefore, menstrual cups should be assessed to determine if they enhance the growth of the bacteria that causes TSS. [40] The recommendations identified in this section are anticipated to address potential risks related to vaginal infection and TSS for menstrual cups.

[38] FDA recommends that as a part of your design validation, you have in place validated test plans for monitoring dioxin and potential pesticide residues for cotton in device materials and final finished devices. We recommend that you evaluate your pad or menstrual cup as described in your test plans and identify the test method and name and address of the testing laboratory in your design history file. You should also explain in your design history file whether testing was conducted on a prototype, on select or all batches, and on a fixed or "as needed" schedule. For more information on design validation and design history files, please see 21 CFR Part 820 Quality Systems, Design Controls (21 CFR 820.30(i)) and Design History File (21 CFR 820.30(j)).

[39] ANSI/AAMI/ISO 14971 *Medical devices—Application of risk management to medical devices*

[40] TSS is not a concern with the use of pads.

Recommendation: As menstrual cups are indwelling in the vagina, there is a potential risk of TSS. For menstrual cups, you should assess the risk of TSS based upon the instructions for use (e.g., dwell time, reprocessing, use life) and materials of construction. A risk analysis based on these factors can help to demonstrate why the risk of TSS is low for your menstrual cup. You should consider device design (e.g., surface area, potential for menstrual cup to facilitate bacterial growth), material biocompatibility and chemical safety, physical impact to vaginal mucosa, and impact to vaginal microbiota when conducting the risk analysis, utilizing supporting information (e.g., literature) to support a lower level of risk of TSS for the menstrual cup.

(3) Non-Clinical Bench Testing

FDA recommends that you have documentation which supports any device performance characteristics described in the labeling for pads or menstrual cups, such as washability or useable life.[41] For menstrual cups, reprocessing validation testing (cleaning and/or disinfection) should be documented to support that the labeling is adequate to ensure appropriate cleaning (or disinfection, if applicable) of the device.

VII. Labeling Recommendations

Labeling for menstrual products should familiarize users with the features of the device, how to use it, and include a description of the device and the materials it contains.

Menstrual products are sold over the counter (OTC) directly to consumers. As OTC devices, under section 502(f) of the FD&C Act and 21 CFR 801.5, the device labeling must include adequate directions for use.[42] The labeling (e.g., package insert) must describe the intended use of the device and include a listing of all conditions, purposes, or uses for which it is recommended, suggested, or commonly used (21 CFR 801.5(a)).

Accurate, clear device labeling is important to make users aware of the risks, limitations, and directions for use of menstrual products. Manufacturers should not make unsubstantiated statements related to the function of any component or purpose of any ingredient. Moreover, a device shall be deemed misbranded if, among other things: its labeling is false or misleading; its labeling does not contain adequate warnings; or any information required to be in the labeling is not prominently placed with such conspicuousness and in such terms to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use (see sections 201(n), 502(a), 502(c), and 502(f)(2) of the FD&C Act).

A. Tampons

The premarket notification must include proposed labeling in sufficient detail to satisfy the

[41] Such documentation should be maintained as part of the design history file. Manufacturers must keep records to the extent required under applicable law, including the QSR (e.g., 21 CFR 820.30(j)), and these (and other) records must generally be made available to an FDA investigator upon request (see section 704(e) of the FD&C Act).

[42] Adequate directions for use means directions under which the layman can use a device safely and for the purposes for which it is intended (21 CFR 801.5).

requirements of 21 CFR 807.87(e). Specifically, proposed labeling, sufficient to describe the tampon, its intended use, and the directions for use must be provided. In addition, tampon labeling must comply with 21 CFR 801.430, "User labeling for menstrual tampons."[43] The recommendations below are intended to help manufacturers develop labeling that complies with applicable labeling requirements for tampons. We intend for these recommendations to supplement and enhance the information that is often already included in labeling for these device types. The requirements described in 21 CFR 801.430 are shown in italic font throughout this section. Labeling recommendations in this guidance are consistent with the requirements of Part 801.

(1) Indications for Use

The labeling (e.g., package insert) must describe the intended use of the device and include a listing of all conditions, purposes, or uses for which it is recommended, suggested, or commonly used (21 CFR 801.5(a)).

For example: The [Trade name] is intended for insertion into the vagina for the absorption of menstrual or other vaginal discharge.

(2) Device Description

The device description in tampon labeling should provide a brief overview of the device and its features in easily understood language.

The device description on the outer package label should identify each ingredient and component of the device. We recommend listing the ingredients of each component separately on the outer package label (i.e., list the pledget, overwrap (cover), removal string and applicator, if any, ingredients separately). This information allows users to individually make informed benefit-risk decisions regarding tampon use. Ingredient information should be presented in a manner that is consistent and easy to access and understand. Ingredient trade names and chemical names may be the most informative way to communicate this information, as trade names may be the most recognizable to the lay population, and the chemical name allows for a more thorough understanding of the specific chemicals present.[44] It is recommended that manufacturers list all ingredients (including fragrances/deodorants) in each component in order of percent of component (highest to lowest). It is also helpful to include a description of the purpose of the ingredient (i.e., what the ingredient does in the product). This helps the user understand why this ingredient has been included in the product.[45] Tables 3a and 3b provide an example ingredient format for tampons:

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[43] Any menstrual tampon that is not labeled as required by paragraphs (c), (d), and (e) of 21 CFR 801.430 and that is initially introduced or initially delivered for introduction into commerce after March 1, 1990, is misbranded under sections 201(n), 502 (a) and (f) of the FD&C Act. See 21 CFR 801.430(h).

[44] See FDA's discussion paper, "Conveying Materials Information about Medical Devices to Patients and Healthcare Providers: Considerations for a Framework."

[45] Scranton, A. *What's in Your Period Product? An investigation of ingredients disclosed on product labels*. Women's Voices for the Earth. 2022. p.9. https://womensvoices.org/report-whats-in-your-period-product/

Table 3a. Sample table format for tampon ingredients.[46]

Tampon	**Function/Purpose**
Absorbent Core	Function of absorbent core
Ingredient 1 (ingredient part a, b, c)	Purpose of ingredient
Ingredient 2	Purpose of ingredient
Tampon Overwrap	Function of overwrap
Ingredient 1	Purpose of ingredient
Ingredient 2	Purpose of ingredient
Withdrawal String	Function of withdrawal string
Ingredient 1	Purpose of ingredient
Ingredient 2	Purpose of ingredient
Applicator	Function of applicator
Ingredient 1	Purpose of ingredient
Ingredient 2	Purpose of ingredient

Table 3b. Sample table format for tampon ingredients with examples.[47]

Tampon	**Function/Purpose**
Absorbent Core	Holds menstrual fluid to prevent leaks
Rayon (cellulose derived from purified wood pulp)	Absorbs menstrual fluid or other vaginal discharge
Cotton (100% organic)	Absorbs menstrual fluid or other vaginal discharge
2,6 Dimethyl-5-Heptenal	Fragrance
Tampon overwrap	Covers the absorbent core and aids in insertion and removal of the tampon
Polyethylene/Polyester	Aids in insertion and removal of the tampon
Withdrawal String	Used to remove the tampon
Polyester	Makes up string core
Cotton	Makes up string core
Paraffin	Anti-wicking agent to prevent withdrawal string from absorbing fluid
Titanium dioxide	Colorant
Applicator	Helps insert the tampon
Polypropylene	Used for applicator barrel and plunger
Pigment Violet 19	Applicator colorant

[46] It is recommended that the information be presented in order of percent of ingredient component (highest to lowest).
[47] *Ibid*

If any animal or plant-derived materials are used, the species and tissue type should be included in the name of animal or plant derived materials, e.g., "contains the following naturally occurring material: cellulose (derived from cotton)". For any mixture or composite materials, you should independently identify each material in parenthesis, e.g., an extract or blend which includes multiple components.

In addition, 21 CFR 801.430 includes requirements related to the device description. Below, following the requirements, we provide recommendations that are intended to help manufacturers develop labeling that complies with the requirement.

21 CFR 801.430(e) states:

> *(e) The statements required by paragraph (e) of this section shall be prominently and legibly placed on the package label of menstrual tampons in conformance with section 502(c) of the Federal Food, Drug, and Cosmetic Act (the act) (unless the menstrual tampons are exempt under paragraph (g) of this section).*[48]
>
> *(1) Menstrual tampon package labels shall bear one of the following absorbency terms representing the absorbency of the production run, lot, or batch as measured by the test described in paragraph (f)(2) of this section;*

*Ranges of absorbency in grams**	*Corresponding term of absorbency*
6 and under	*Light absorbency*
6 to 9	*Regular absorbency*
9 to 12	*Super absorbency*
12 to 15	*Super plus absorbency*
15 to 18	*Ultra absorbency*
Above 18	*No term*

> ** These ranges are defined, respectively, as follows: Less than or equal to 6 grams (g); greater than 6 g up to and including 9 g; greater than 9 g up to and including 12 g; greater than 12 g up to and including 15 g; greater than 15 g up to and including 18 g; and greater than 18 g.*
>
> *(2) The package label shall include an explanation of the ranges of absorbency and a description of how consumers can use a range of absorbency, and its corresponding absorbency term, to make comparisons of absorbency of tampons to allow selection of the tampons with the minimum absorbency needed to control menstrual flow in order to reduce the risk of contracting TSS.*

Recommendation: The package label should include a device description with information on selection of device size and absorbency. In order to appropriately label the device absorbency per

[48] In accordance with paragraph (g) of 21 CFR 801.430, any menstrual tampon intended to be dispensed by a vending machine is exempt from the requirements of this section.

21 CFR 801.430(e), refer to Section VI.C.(1).a of this guidance for recommendations related to the testing described in 21 CFR 801.430(f)(2).

(3) Warnings

We recommend that you include a warning statement about allergic reactions and irritation, for example:

- If an allergic reaction or irritation occurs from using [device], you should discontinue use and consult a health care provider.

In addition, 21 CFR 801.430 includes requirements related to warnings. Below, following each requirement, we provide recommendations that are intended to help manufacturers develop labeling that complies with the requirement.

21 CFR 801.430(d) states:

> *(d) The labeling of menstrual tampons shall contain the following consumer information prominently and legibly, in such terms as to render the information likely to be read and understood by the ordinary individual under customary conditions of purchase and use:*

Recommendation: We recommend that manufacturers prominently display appropriate warnings in the instructions for use regarding how to avoid known hazards associated with the use of the tampon.

21 CFR 801.430(d)(1) states:

> *(1)*
>
> *(i) Warning signs of TSS, e.g., sudden fever (usually 102° or more) and vomiting, diarrhea, fainting or near fainting when standing up, dizziness, or a rash that looks like a sunburn;*
>
> *(ii) What to do if these or other signs of TSS appear, including the need to remove the tampon at once and seek medical attention immediately;*

Recommendations: In order to communicate the warning signs of TSS, the labeling should include:

- A statement that symptoms and signs of TSS may include a sudden fever (usually 102°F or more), vomiting, diarrhea, fainting or feeling like you are going to faint when standing up, dizziness, or a rash that looks like a sunburn.
- A statement to know the signs of TSS and how to reduce your risk.
- A statement to immediately remove the tampon and contact your health care provider if you have pain, fever or other unusual symptoms.

21 CFR 801.430(d)(2) states:

(2) The risk of TSS to all women using tampons during their menstrual period, especially the reported higher risks to women under 30 years of age and teenage girls, the estimated incidence of TSS of 1 to 17 per 100,000 menstruating women and girls per year, and the risk of death from contracting TSS;

Recommendation: In order to communicate the risk of TSS, the labeling should include a warning statement to inform users of the estimated incidence of TSS.

21 CFR 801.430(d)(3) states:

(3) The advisability of using tampons with the minimum absorbency needed to control menstrual flow in order to reduce the risk of contracting TSS;

Recommendation: The labeling should include a warning statement to use the lowest absorbency tampon needed.

21 CFR 801.430(d)(4) states:

(4) Avoiding the risk of getting tampon-associated TSS by not using tampons, and reducing the risk of getting TSS by alternating tampon use with sanitary napkin use during menstrual periods; and

Recommendations: In order to communicate the above information about reducing the risk of getting TSS, the labeling should include:

- A warning to follow all labeled directions for use;
- A warning to limit wear-time per tampon to no more than 8 hours;
- A warning to advise against the use of tampons "overnight";
- A warning to wash your hands before and after using a tampon; and
- A warning to use tampons only when you have your menstrual cycle (period).

21 CFR 801.430(d)(5) states:

(5) The need to seek medical attention before again using tampons if TSS warning signs have occurred in the past, or if women have any questions about TSS or tampon use.

Recommendation: To communicate the risk of recurrent TSS, the labeling should include a warning statement to seek medical attention to make an informed decision on device use, especially in situations where signs of TSS have previously occurred.

21 CFR 801.430(c) states:

(c) If the information specified in paragraph (d) of this section is to be included as a package insert, the following alert statement shall appear prominently and legibly on the package label:

ATTENTION: Tampons are associated with Toxic Shock Syndrome (TSS). TSS is a rare but serious disease that may cause death. Read and save the enclosed information.

Recommendation: No additional recommendations for this labeling requirement.

(4) Additional Considerations for the Directions for Use

The directions for use should include information on tampon insertion, how the tampon should be worn, wear time, removal, and disposal. Information related to how the device is intended to be used should be noted (e.g., single use, use in specific populations, and intended users).

B. Pads and Menstrual Cups

Labeling for pads and menstrual cups should familiarize users with the features of the device, how to use it, and include a description of the device and the materials it contains.

(1) Indications for Use

The labeling (e.g., package insert) must describe the intended use of the device and include a listing of all conditions, purposes, or uses for which it is recommended, suggested, or commonly used (21 CFR 801.5(a)).

For example (pad): The [Trade name] is an external pad intended for absorption of menstrual or other vaginal discharge.

For example (menstrual cup): The [Trade name] is a receptacle placed in the vagina to collect blood and cellular debris that is extruded from the uterus via the cervix during menstruation.

(2) Device Description

The device description should provide a brief overview of the device and its features in easily understood language. This should include information on selection of device size and, for menstrual cups, the volume of menstrual fluid that the cup can hold for the stated duration of use.

The device description on the outer package label should identify each ingredient or component of the device. We recommend listing the ingredients of each component separately on the outer package label (e.g., list the cup, applicator and pusher, if any, ingredients separately for a menstrual cup). This information allows users to individually make informed benefit-risk decisions regarding device use. Ingredient information should be presented in a manner that is consistent and easy to access and understand. Ingredient trade names and chemical names may be the most informative way to communicate this information, as trade names may be the most recognizable to the lay population, and the chemical name allows for a more thorough understanding of the specific chemicals present.[49] Manufacturers should list all the ingredients (including fragrances/deodorants) in each component in order of percent of component (highest to lowest). It is also helpful to include a description of the purpose of the ingredient (i.e., what

[49] See FDA's discussion paper, "Conveying Materials Information about Medical Devices to Patients and Healthcare Providers: Considerations for a Framework."

the ingredient does in the product). This helps the user understand why this ingredient has been included in the product.[50] Tables 4a and 4b provide an example ingredient format for pads and Tables 5a and 5b provide an example ingredient formant for menstrual cups:

Table 4a. Sample table format for pad ingredients.[51]

Pad	**Function/Purpose**
Absorbent Core	Function of absorbent core
Ingredient 1 (ingredient part a, b, c)	Purpose of ingredient
Ingredient 2	Purpose of ingredient
Ingredient 3	Purpose of ingredient
Ingredient 4	Purpose of ingredient
Plastic film/Top sheet	Function of plastic film
Ingredient 1	Purpose of ingredient
Back sheet with adhesive	Function of back sheet with adhesive
Ingredient 1	Purpose of ingredient
Ingredient 2	Purpose of ingredient

Table 4b. Sample table format for pad ingredients with examples.[52]

Pad	**Function/Purpose**
Absorbent Core	Holds menstrual fluid to prevent leaks
Rayon (cellulose derived from purified wood pulp)	Absorbs menstrual fluid or other vaginal discharge
Cotton (100% organic)	Absorbs menstrual fluid or other vaginal discharge
Synthetic musks	Fragrance
Super absorbent gel (sodium polyacrylate crystals)	Chemical absorbing polymer that turns into a gel when exposed to moisture
Plastic film/Top sheet	Encloses absorbent core and allows fluid to pass through quickly
Polyolefin	Used to make plastic film for top sheet
Back sheet with adhesive	Prevents leakage of absorbent core and maintains position by attachment to underwear
Polyethylene film	Used to make plastic film for back sheet
Hot Melt Adhesive	Adhesive for attachment

[50] Scranton, A. *What's in Your Period Product? An investigation of ingredients disclosed on product labels*. Women's Voices for the Earth. 2022. p.9. https://womensvoices.org/report-whats-in-your-period-product/

[51] It is recommended that the information be presented in order of percent of ingredient component (highest to lowest).

[52] *Ibid*

Table 5a. Sample table format for menstrual cup ingredients.[53]

Menstrual Cup	**Function/Purpose**
Menstrual Cup	Function of menstrual cup
Ingredient 1	Purpose of ingredient
Ingredient 2	Purpose of ingredient
Ingredient 3	Purpose of ingredient
Ingredient 4	Purpose of ingredient
Applicator	Function of applicator
Ingredient 1	Purpose of ingredient
Ingredient 2	Purpose of ingredient
Ingredient 3	Purpose of ingredient
Pusher	Function of pusher
Ingredient 1	Purpose of ingredient

Table 5b. Sample table format for menstrual cup ingredients with examples.[54]

Menstrual Cup	**Function/Purpose**
Menstrual Cup	Receptacle to collect blood and cellular debris that is extruded from the uterus via the cervix during menstruation
Silicone	Primary material of the cup
Parylene C	Lubricant coating
Applicator	Helps insert the cup
TPU: Pellethane	Primary material of applicator tip
Nylon	Primary material of applicator barrel
FDA Pale Lilac 2085C Concentrate	Applicator colorant
Pusher	Helps in deployment
Polypropylene	Used to make pusher base

If any animal or plant-derived materials are used, the species and tissue type should be included in the name of animal or plant derived materials, e.g., "contains the following naturally occurring material: cellulose (derived from cotton)". For any mixture or composite materials, you should independently identify each material in parenthesis, e.g., an extract or blend which includes multiple components.

[53] It is recommended that the information be presented in order of percent of ingredient component (highest to lowest).

[54] *Ibid*

(3) Warnings

We recommend that manufacturers prominently display appropriate warnings in the instructions for use regarding how to avoid known hazards associated with the use of the pad or menstrual cup.

We also recommend that you include a warning statement about allergic reactions and irritation, for example:

- If an allergic reaction or irritation occurs from using [device], you should discontinue use and consult a health care provider.

(4) Additional Considerations for the Directions for Use

The directions for use should include information on insertion (for menstrual cups), how the products should be worn, wear time, removal, reuse (if applicable), and disposal. Information related to how the device is intended to be used should be noted (e.g., single or multiple use, use in specific populations, and intended users).

VIII. Modifications (Devices subject to 510(k) requirements)[55]

In accordance with 21 CFR 807.81(a)(3), a device change or modification "that could significantly affect the safety or effectiveness of the device" or represents "a major change or modification in the intended use of the device" requires a new 510(k).[56] The changes or modifications listed below are examples of changes that may require submission of a new 510(k), but note that this list is not exhaustive. For additional details, see FDA guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device."

[55] Although this section is focused on devices that are subject to 510(k) requirements, devices which are typically exempt from premarket notification procedures remain subject to the limitations in 21 CFR 884.9. In situations where the limitations to the exemption are exceeded (e.g., device intended for a different use, modified device operates using a different fundamental scientific technology) as expressly identified in 21 CFR 884.9, the manufacturer would need to submit a 510(k) and get clearance prior to marketing such device.

[56] Section 3308 of the Food and Drug Omnibus Reform Act of 2022 (FDORA), enacted as part of the Consolidated Appropriations Act, 2023, added section 515C "Predetermined Change Control Plans for Devices" to the FD&C Act (Pub. L. No. 117-328). Section 515C has provisions regarding predetermined change control plans (PCCPs) for devices requiring premarket approval or premarket notification. For example, section 515C states that supplemental applications (section 515C(a)) and new premarket notifications (section 515C(b)) are not required for a change to a device that would otherwise require a premarket approval supplement or new premarket notification if the change is consistent with a PCCP approved or cleared by FDA. Section 515C also states that FDA may require that a PCCP include labeling for safe and effective use of a device as such device changes pursuant to such plan, notification requirements if the device does not function as intended pursuant to such plan, and performance requirements for changes made under the plan. If you are interested in proposing a PCCP in your marketing submission, we encourage you to submit a Pre-Submission to engage in further discussion with CDRH. See FDA's guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program."

Examples of such changes or modifications include:

- Modifying the indications for use by changing the indications for use from collection of menstrual or other vaginal discharge, which could change form, fit and/or clinical performance – FDA generally considers this to be a significant change or modification to the labeling. This type of change could significantly affect the safety or effectiveness of the device.

- New device materials or additives– FDA generally considers this to be a significant change as this type of change (e.g., changes to the pledget material or overwrap to a new material) could significantly affect the safety of the device and additional evidence may be needed to demonstrate substantial equivalence. However, minor changes in the ratio of materials utilized in a previously cleared tampon that do not raise any new or increased biocompatibility concerns based on a risk assessment or affect performance specifications (e.g., changing absorbent material in tampon pledget from a 50/50 cotton and rayon blend to 80/20 blend), would likely not require submission of a new 510(k).

- Modifications resulting in a design that is dissimilar (e.g., a significant change in pledget design/geometry) from the design of legally marketed devices – FDA generally considers this to be a significant change or modification in design. This type of change could significantly affect the effectiveness of the device and/or alter the safety profile by introducing new or additional risk factors.

- Modification to achieve a 15-18 gram or above 18 gram absorbency (as demonstrated by Syngyna test, as defined in 21 CFR 801.430(f)(2)) where the original device had a lower absorbency – FDA generally considers this to be a significant change or modification in design. This type of change could significantly affect the safety and effectiveness of the device and additional performance testing may be needed to demonstrate substantial equivalence. A modification in design that would add an absorbency range other than "ultra" (15-18 gram) or above 18 grams consistent with the absorbency ranges specified in 21 CFR 801.430(e)(1), would likely not require submission of a new 510(k) as such a modification generally would not be expected to affect the safety or effectiveness of the device and would not be a major change or modification in the intended use of the device.

When a modification does not affect the intended use or alter the fundamental scientific technology of the device but requires a new 510(k) in accordance with 21 CFR 807.81(a)(3), FDA recommends you submit a Special 510(k).[57]

In any 510(k) for a change or modification to a legally marketed tampon, we recommend that you describe the modification and its effects and provide supporting information (such as a risk analysis, performance characteristics, or non-clinical or clinical information) demonstrating that the modification does not adversely affect safety or effectiveness.

[57] Refer to the FDA guidance, "The Special 510(k) Program" for more information.

Guidance History*	Date	Description
Reissued as Level 1 Draft Guidance	October 2025	See Notice of Availability for more information.**
Level 1 Final Guidance	July 2005	See Notice of Availability for more information.**

*This table was implemented beginning February 2025 and previous guidance history may not be captured in totality.

**The Notice of Availability is accessible via the Search for FDA Guidance Documents webpage.