Classification of Absorbable Synthetic Wound Dressings

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Device Description

An absorbable synthetic wound dressing is a device intended to cover a wound, to absorb exudate, and to maintain appropriate moisture balance within the wound.

- Composed of absorbable synthetic materials (e.g., lactide-caprolactone copolymer, biodegradable polyurethane), often presented as a fibrous matrix.
  - Does not contain animal-derived materials, antimicrobials, drugs, or biologics.
- Covers a wound, reduces dressing change frequency, or provides a temporary scaffold for cellular infiltration.
- Completely or partially degrades in wound.
- Used alone or in conjunction with a secondary, non-resorbable wound dressing.
- Not intended as a long-term skin substitute, a temporary synthetic skin, or to accelerate the wound healing process.

Indications for Use

These devices have been cleared as prescription use devices for the following representative indications for use:

- Temporary coverage of non-infected superficial wounds
- Maintain a moist wound healing environment
- Management of wounds, including:
  - Partial and full thickness wounds
  - Pressure (stage I - IV) ulcers
  - Venous ulcers
  - Ulcers caused by mixed vascular etiologies
  - Venous stasis ulcers
  - Chronic vascular ulcers
  - Diabetic ulcers
  - Tunneled/undermined wounds
  - Partial thickness burns
  - Trauma wounds
  - Cuts
  - Acute wounds
  - Surgical wounds
  - Superficial wounds
  - Draining wounds

Regulatory History

- Absorbable synthetic wound dressings are a pre-amendments, unclassified device type (i.e., have been in commercial distribution prior to May 28, 1976).

- Currently these devices are being regulated through the 510(k) pathway and are cleared for marketing if their intended use and technological characteristics are “substantially equivalent” to a legally marketed predicate device. Since these devices are unclassified, there is no regulation associated with the product code.

    - Absorbable synthetic wound dressings are subset of devices currently cleared under product code "FRO.”

- To date, the FDA has cleared 11 devices currently under the FRO product code.

Clinical Background

Disease Characteristics

- Wide variety of acute and chronic wounds.
- Acute wounds usually occur suddenly and heal at a predictable rate; these include cuts, post-surgical wounds, burns, and traumatic wounds. An acute wound can sometimes develop into a chronic wound.
- Chronic wounds develop over time and do not heal at an expected rate. The most common chronic wounds are venous ulcers, diabetic ulcers, and pressure ulcers.

Pathophysiology

- Varied, depends on many factors, including blood supply, blood pressure, infection, and other comorbidities (e.g., diabetes).

Patient Outcomes

- Patient history, physical examination, and laboratory studies including bloodwork, cultures, and radiologic imaging may be used to ascertain the wound diagnosis.
- Depending on the wound type, the patient may be asked about pain, functional status, and quality of life.

Clinical Background

Currently Available Treatment

- There is a range of standard of care methods, depending on the wound type and wound healing progression.

- Variety of other wound care modalities available, including
  - compressive dressings
  - bioengineered dressings
  - grafts
  - negative pressure wound therapy
  - pressure relief devices
  - hyperbaric oxygen
  - topical drugs

- General recommendations from national and international organizations: debridement, rinsing, and providing a moist wound environment as part of wound care.

Literature Review

- A systematic literature review (SLR) was conducted in an effort to gather any published information regarding the safety and effectiveness of Absorbable Synthetic Wound Dressings
- SLR searches were conducted to identify any relevant articles published between April 1, 2012, and July 18, 2022 .
- The SLR searches were limited to full text publications in English and human clinical studies with N < 75 patients per arm excluded.
- The SLR searches yielded a total of 5018 initial literature references for absorbable synthetic wound dressings together with wound dressings with animal-derived materials and hemostatic wound dressings with and without thrombin.
- No articles from the SLR searches were determined to be relevant to the safety and/or effectiveness of Absorbable Synthetic Wound Dressings.
- A supplemental search was conducted with removal of patient number limitation and 7 relevant articles were identified.

Literature Review – Safety Assessment

- 4 of the 7 articles reported on device safety:
  - No significant difference from the SOC group (collagen dressing) in complications of infection, dehiscence, and hematoma or seroma. (*Wu et al., 2022*)
  - Less incidence of adverse events and infection of index ulcer than the SOC group (collagen alginate dressing) in diabetic foot ulcer care. (*Armstrong et al., 2022*)
  - No allergic reactions or infections identified with the use of absorbable synthetic wound dressings. (*Schwarze, et al., 2008; Keck, et al., 2012*)

Literature Review – Effectiveness Assessment

- All the 7 articles reported on device effectiveness for the following uses:
  - In the staged reconstruction of complex wounds as a temporary covering and scaffold (2 studies)
  - In diabetic foot ulcer care (1 study)
  - In second-degree burns and skin graft donor sites (2 studies)
  - In deep partial-thickness dermal wounds (1 study)
  - In donor sites of split-thickness skin grafts (1 study)

Literature Review – Effectiveness Assessment

- In the 2 studies for staged reconstruction of complex wounds
  - One study reported significantly lower rate of later skin graft failure than the SOC group (collagen) (*Wu et al., 2022*)
  - One study reported high integration rate of dressings into wounds (*Li et al., 2021*)
- In the study for diabetic foot ulcer care (*Armstrong et al. 2022)*
  - Percentage wound area reduction at 12-weeks: 79% for test group vs 37% for SOC (collagen alginate dressing)
  - Neuropathic score at 12-weeks: 2.0 for test group vs –0.6 for SOC
- In the two studies for second-degree burns and skin graft donor sites (*Schwarze, et al., 2008; Schwarze, et al., 2007*)
  - Similar healing time and re-epithelization as SOC (hydrophilic polyurethane membrane and paraffin gauze
- In the study for deep partial-thickness dermal wounds (*Keck, et al., 2012*)
  - Similar scar formation and scar quality as SOC (split-thickness skin graft)
- In the study for donor sites of split-thickness skin grafts (*Kaartinen, et al., 2011*)
  - Similar epithelialization, but less pain and bleeding than SOC (polyurethane foam coated with silicone elastomer)

Literature Review – Conclusions

- The selected studies from published literature did not report additional risks or adverse events associated with absorbable synthetic wound dressings as compared with the SOC groups.
- The absorbable synthetic wound dressings had similar complication rate, healing time and re-epithelization in the treatment of different wound types when compared to the SOC groups.
- Limitations of the literature review:
  - Limited publications
  - Limited patient number (15-97 patients)
  - Only 3 studies (3/7) were randomized, controlled trials (RCT)

Medical Device Reports

- Medical Device Reporting (MDR): the mechanism for the FDA to receive significant medical device adverse events from:
  - mandatory reporters (manufacturers, importers and user facilities)
  - voluntary reporters (health care professionals, patients, consumers)

Medical Device Reports

- MDR reports can be used effectively to:
  - Establish a qualitative snapshot of adverse events for a specific device or device type
  - Detect actual or potential device problems used in a “real world” setting/environment, including:
    - rare, serious, or unexpected adverse events
    - adverse events that occur during long-term device use
    - adverse events associated with vulnerable populations
    - off-label use
    - user error

Medical Device Reports

- Limitations
  - Under reporting of events
  - Potential submission of incomplete, inaccurate, untimely, unverified, or biased data
  - Incidence or prevalence of an event cannot be determined from this reporting system alone
  - Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report
  - MAUDE data does not represent all known safety information for a reported medical device

Medical Device Reports

- MAUDE (Manufacturer And User Facility Device Experience) Database reviewed for the brand names from the database start through April 1, 2022:
  - 10 MDR reports returned: 8 reports for serious injury; 2 reports for death.
  - Reporting countries: US - 5; OUS -5
  - All 10 MDR reports were submitted by the manufacturers

Medical Device Reports

Adverse Events	Count
Alteration in Body Temperature	3
Insufficient Information	2
Pleural Effusion	1
Hemorrhage/Bleeding	1
Hematoma	1
Congestive Heart Failure	1
Cancer	1
Hyperthermia	1
Death	1
Appropriate Clinical Signs, Symptoms, Conditions Term / Code Not Available	1
Respiratory Failure	1
Failure of Implant	1

Recall History

- The Medical Device Recall database contains medical device recalls classified since November 2002.
- Since January 2017, it may also include correction or removal actions initiated by a firm prior to review by the FDA.
- The status is updated if the FDA identifies a violation and classifies the action as a recall and again when the recall is terminated.
- FDA recall classification (resulting in the posting date) may occur after the firm recalling the medical device product conducts and communicates with its customers about the recall.

Recall History

- Medical Device Recall Database was queried for product code “FRO” and brand names of cleared absorbable synthetic wound dressings (August 18, 2022):
  - One Class II* recall identified
  - Initiated due to misprinted expiration date on the device packaging.

- The identified recall appears to be due to manufacturing error and does not suggest additional risks associated with absorbable synthetic wound dressings as a product class.

*A Class II recall is a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Risks and Mitigations

Identified Risk	Description/Examples	Recommended Mitigation Measure
Toxicity	This can result from device materials or degradants of the absorbable materials, which can be toxic.	• Biocompatibility evaluation • Performance testing • Labeling
Adverse Tissue Reaction	This can result from the use of device materials, including any associated impurities, residues and degradants, which are not biocompatible.	• Biocompatibility evaluation • Performance testing and descriptive information • Pyrogenicity testing • Labeling
Infection	This can result from inadequate device sterilization or inadequate packaging integrity.	• Sterilization testing/validation information • Shelf-life validation • Labeling
Delay in wound healing	This can result from device materials or degradants of the absorbable materials, which may interfere with the wound healing process. This can also result from incomplete bio-resorption of the dressing into the wound.	• Biocompatibility evaluation • Animal performance testing • Performance testing and descriptive information • Labeling
Failure of device integration	This occurs when the dressing, which is intended to provide a temporary scaffold for cellular infiltration, does not effectively degrade in the wound, and thus resulting in dressing retention in the wound and interference with the wound healing process.	• Animal performance testing • Performance testing • Labeling

Proposed Classification

878.4023 Absorbable Synthetic Wound Dressings.

(a) *Identification.* An absorbable synthetic wound dressing is a device intended to cover a wound, to absorb exudate, and to maintain appropriate moisture balance within the wound. These devices may additionally be intended as a scaffold for cellular infiltration. It is composed of absorbable synthetic materials, such as biodegradable polymers. Absorbable synthetic wound dressings may be used alone or in conjunction with a secondary, non-resorbable wound dressing for securement. An absorbable synthetic wound dressing is not intended as a long-term skin substitute, a temporary synthetic skin, or to accelerate the wound healing process. An absorbable synthetic wound dressing does not contain animal-derived materials, antimicrobials, drugs, or biologics.

(b) *Classification.*
Class II (special controls).

Proposed Special Controls

Based on the identified risks and recommended mitigation measures, FDA believes that the following special controls would provide reasonable assurance of safety and effectiveness for the for absorbable synthetic wound dressings:

1. Performance testing and descriptive information must demonstrate the functionality of the device to achieve the specified use, including establishing the physical and chemical characteristics of the device. The following must be provided:
    i. Identity, quantification, and purpose of each component in the finished product;
    ii. Specification and characterization of each component in the finished product; and
    iii. Final release specifications for the finished product.
2. Performance data must demonstrate the sterility of the device.
3. The device, including any degradants, must be demonstrated to be biocompatible, non-pyrogenic and contain endotoxin level within acceptable limits.
4. Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.
5. Animal performance testing must demonstrate that the device materials and degradants do not delay the wound healing process and can be appropriately integrated into the surrounding tissues.

Proposed Special Controls

6. Performance data must demonstrate that the device performs as intended under anticipated conditions of use, including complete degradation of any absorbable material(s) in the wound and evaluation of expected worst-case conditions.
7. The labeling must include:
    i. A description of the intended user population.
    ii. Specific instructions regarding the proper placement, sizing, duration of use, frequency of dressing change, maximum use life per application of the dressing, maximum total use life of the dressing, and removal of the dressing, if applicable.
    iii. A list of each ingredient or component within the finished device, including the functional role of that ingredient or component within the device.
    iv. If the device has non-resorbable components, a warning statement for the potential retention of those components in the wound or the surrounding area.
    v. A contraindication for any known sensitivity to components within the device.

Proposed Special Controls

vi. A contraindication if there are incompatibilities with other therapies.

vii. A shelf life.

viii. A statement regarding when to discontinue use of the device after multiple reapplications based on biocompatibility and performance testing, if applicable.

ix. 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 covering a wound, absorbing exudate, and maintaining appropriate moisture balance within the wound.

x. Disposal instructions.

U.S. FOOD & DRUG ADMINISTRATION

Thank You

Questions to Panel – Absorbable Synthetic Wound Dressings

Min Zhang, Lead Reviewer, OHT4

Question 1 to Panel

FDA has identified in the following table risks to health for absorbable synthetic wound dressings.

Question 1 to Panel

Identified Risk	Description/Examples
Toxicity	This can result from device materials or degradants of the absorbable materials, which can be toxic.
Adverse tissue reaction	This can result from the use of device materials, including any associated impurities, residues and degradants, which are not biocompatible.
Infection	This can result from inadequate device sterilization or inadequate packaging integrity.
Delays in wound healing	This can result from device materials or degradants of the absorbable materials, which may interfere with the wound healing process. This can also result from incomplete bio-resorption of the dressing into the wound.
Failure of device integration	This occurs when the dressing, which is intended to provide a temporary scaffold for cellular infiltration, does not effectively degrade in the wound, and thus resulting in dressing retention in the wound and interference with the wound healing process.

Question 1 to Panel

Please comment on whether you agree with inclusion of all the risks in the overall risk assessment of absorbable synthetic wound dressings.

In addition, please comment on whether you believe that any additional risks should be included in the overall risk assessment of these absorbable synthetic wound dressings.

Question 2 to Panel

Section 513 of the Food, Drug, and Cosmetic Act states a device should be Class III if:

- insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of its safety and effectiveness, AND
- the device is purported or represented to be for a use in supporting or sustaining human life, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

A device should be Class II if:

- general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness, AND
- there is sufficient information to establish special controls to provide such assurance.

Question 2 to Panel

A device should be Class I if:

- general controls are sufficient to provide reasonable assurance of the safety and effectiveness, OR
- insufficient information exists to:
  - determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness, OR
  - establish special controls to provide such assurance, BUT
    - is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, AND
    - does not present a potential unreasonable risk of illness or injury.

Question 2 to Panel

FDA believes general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness and sufficient information exists to establish special controls to adequately mitigate the risks to health and provide reasonable assurance of device safety and effectiveness for this device type.

As such, FDA believes that Class II is the appropriate classification for absorbable synthetic wound dressings.

Question 2 to Panel

Identified Risk	Recommended Mitigation Measure
Toxicity	Biocompatibility evaluation, Performance testing, Labeling
Adverse tissue reaction	Biocompatibility evaluation, Performance testing, descriptive information, Pyrogenicity testing, Labeling
Infection	Sterilization testing/validation information, Shelf-life validation, Labeling
Delays in wound healing	Biocompatibility evaluation, Animal performance testing, Performance testing, descriptive information, Labeling
Failure of device integration	Animal performance testing, Performance testing, Labeling

Question 2 to Panel

Please discuss whether the identified special controls for absorbable synthetic wound dressings appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

Proposed Special Controls

1. Performance testing and descriptive information must demonstrate the functionality of the device to achieve the specified use, including establishing the physical and chemical characteristics of the device. The following must be provided:
    i. Identity, quantification, and purpose of each component in the finished product;
    ii. Specification and characterization of each component in the finished product; and
    iii. Final release specifications for the finished product.
2. Performance data must demonstrate the sterility of the device.
3. The device, including any degradants, must be demonstrated to be biocompatible, non-pyrogenic and contain endotoxin level within acceptable limits.
4. Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.
5. Animal performance testing must demonstrate that the device materials and degradants do not delay the wound healing process and can be appropriately integrated into the surrounding tissues.

Question 2 to Panel

Please discuss whether the identified special controls for absorbable synthetic wound dressings appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

Proposed Special Controls

6. Performance data must demonstrate that the device performs as intended under anticipated conditions of use, including complete degradation of any absorbable material(s) in the wound and evaluation of expected worst-case conditions.
7. The labeling must include:
    i. A description of the intended user population.
    ii. Specific instructions regarding the proper placement, sizing, duration of use, frequency of dressing change, maximum use life per application of the dressing, maximum total use life of the dressing, and removal of the dressing, if applicable.
    iii. A list of each ingredient or component within the finished device, including the functional role of that ingredient or component within the device.
    iv. If the device has non-resorbable components, a warning statement for the potential retention of those components in the wound or the surrounding area.
    v. A contraindication for any known sensitivity to components within the device.

Question 2 to Panel

Please discuss whether the identified special controls for absorbable synthetic wound dressings appropriately mitigate the identified risks to health and whether additional or different special controls are recommended.

Proposed Special Controls

vi. A contraindication if there are incompatibilities with other therapies.

vii. A shelf life.

viii. A statement regarding when to discontinue use of the device after multiple reapplications based on biocompatibility and performance testing, if applicable.

ix. 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 covering a wound, absorbing exudate, and maintaining appropriate moisture balance within the wound.

x. Disposal instructions.

Question 3 to Panel

Please discuss whether you agree with FDA's proposed classification of Class II with special controls for absorbable synthetic wound dressings.

If you do not agree with FDA's proposed classification, please provide your rationale for recommending a different classification.

End of Panel Questions for Absorbable Synthetic Wound Dressings

Min Zhang, Lead Reviewer, OHT4