U.S. FOOD & DRUG ADMINISTRATION

General and Plastic Surgery Devices Panel of the Medical Devices Advisory Committee

Classification of Wound Dressings Combined with Drugs

September 20-21, 2016

Sep 21: Classification

Device Classification

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What Is the Purpose of This Panel Meeting?

- Discuss the indications for use, risks to health, and safety and effectiveness of wound dressings combined with drugs, currently a pre-amendment, unclassified device type with the product code FRO
- Provide input to FDA on the classification of wound dressings combined with drugs: Class III, Class II, or Class I

What Is a Preamendments Device?

A device of a type that was introduced into interstate commerce prior to May 28, 1976 (the enactment date of the Medical Device Amendments)

What Is an Unclassified Device?

A preamendments device that was not classified by the original classification panels; therefore, no classification regulation currently exists for this device type.

What Is the Classification Process for Preamendment, Unclassified Devices?

- Preamendment devices are classified after FDA has:
  - Received a recommendation from a device Classification Panel
  - Published the Panel's recommendation for comment, along with a proposed rule classifying the device; and
  - Published a final rule classifying the device

What Are the Device Classes?

Class I	Class II	Class III
• General Controls • Low to moderate risk	• General and Special Controls • Moderate to high risk	• General controls and Premarket Approval (PMA) • High risk

Class I Devices

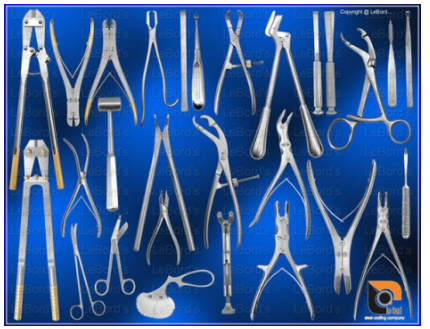
- Devices for which general controls are sufficient to provide reasonable assurance of the safety and effectiveness
- Typically do not require premarket review by the FDA prior to being marketed

What Are General Controls?

- General Controls include:
  - Prohibition against adulterated or misbranded devices,
  - Good Manufacturing Practices (GMPs),
  - Registration of manufacturing facilities,
  - Listing of device types,
  - Recordkeeping, etc.

What Are Some Examples of Class I Devices?

- General Surgical Instruments
- Surgical Gloves
- Medical Adhesive Tape



Class I Devices

- Devices which cannot be classified into Class III:
  - Because they are not life sustaining, life supporting, of substantial importance in preventing impairment of public health, and
  - Because they do not present a potential unreasonable risk of illness or injury
- Devices which cannot be classified into Class II:
  - Because insufficient information exists to establish special controls to provide a reasonable assurance of safety and effectiveness

What Are Class II Devices?

- Cannot be classified into Class I:
  - because general controls are insufficient to provide reasonable assurance of the safety and effectiveness of such device, and
  - for which there is sufficient information to establish special controls to provide such assurance

- Class II devices typically require premarket notification to FDA (i.e., a 510(k)) prior to being marketed

What Are Special Controls?

- Special Controls include:
  - Performance standards
  - Postmarket surveillance
  - Patient registries
  - Special labeling requirements
  - Development and dissemination of guidelines, etc.

How Are Special Controls Used?

- As an example, tissue adhesive for the topical approximation of skin devices were reclassified from Class III to Class II (special controls)
- FDA issued a special controls guidance to mitigate risks to health:
  - Biocompatibility testing
  - Material characterization
  - Chemistry
  - Bench testing (adhesive strength, degradation rate, etc.)
  - Sterility
  - Labeling (warnings, precautions, adverse effects, etc.)
  - Animal and Clinical testing
- These special controls, in combination with the general controls, provide reasonable assurance of safety and effectiveness
- Companies must provide evidence in their 510(k) submissions of how the special controls were addressed

What Are Some Examples of Class II Devices?

- Surgical Suture
- Fetal Heart Monitor
- Gastrointestinal Feeding Tube
- Hemodialysis System

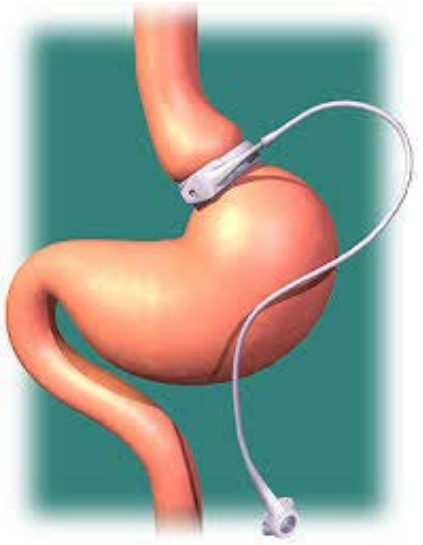
What Are Class III Devices?

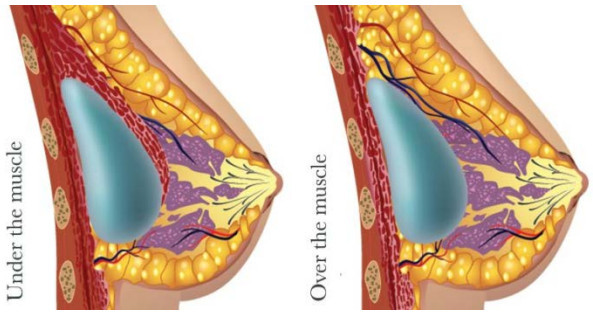
- Cannot be classified into Class II because:
  - insufficient information exists to determine that general and specials controls are sufficient to provide reasonable assurance of the safety and effectiveness, and
  - The devices are:
    - life sustaining and/or life supporting, or
    - of substantial importance in preventing impairment of human health; or
    - presents potential unreasonable risk of illness or injury

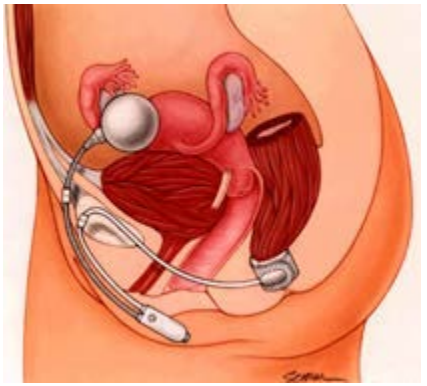
- Class III devices typically require premarket approval (PMA) prior to being marketed

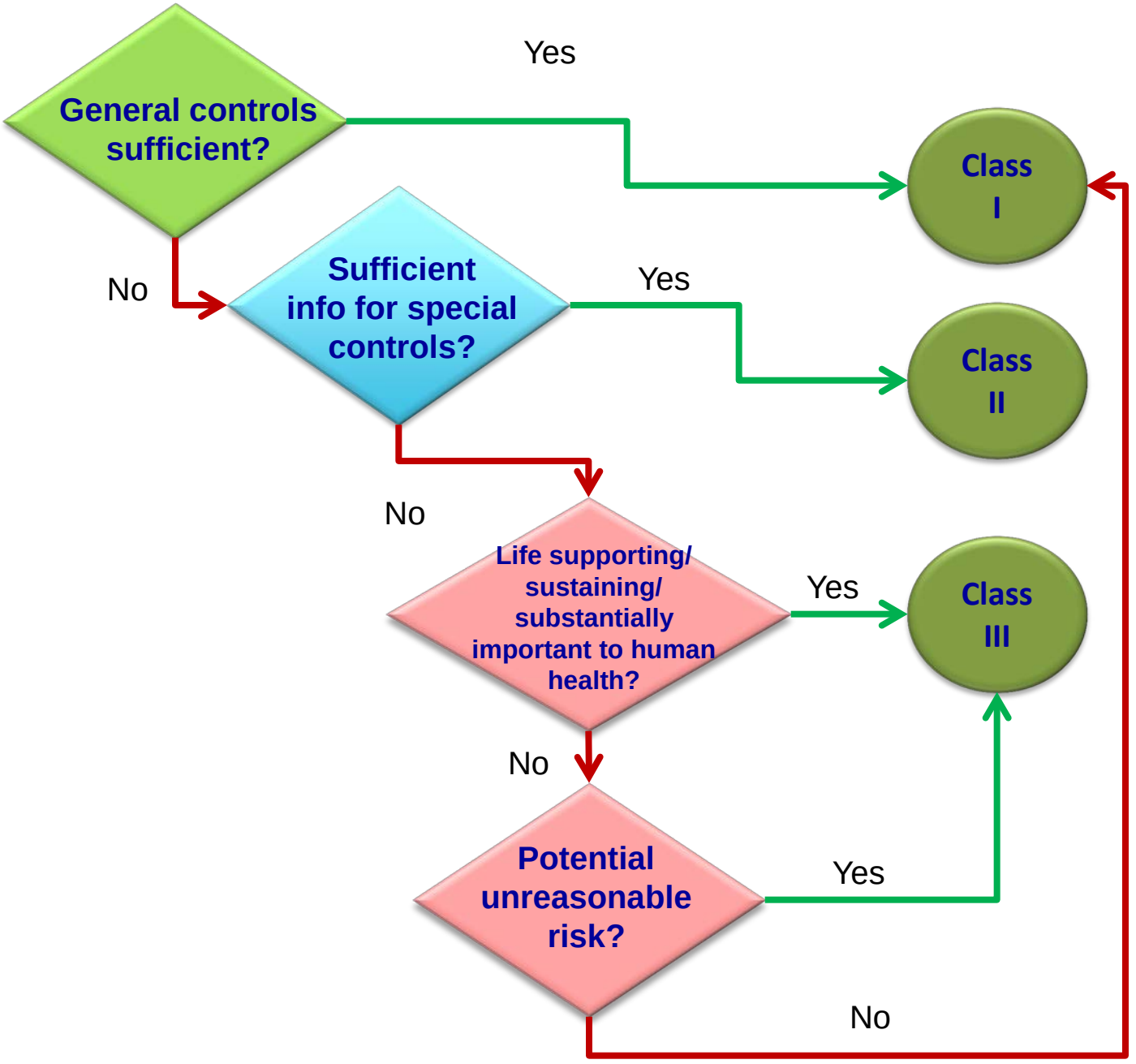
What Are Some Examples of Class III Devices?

- Breast Implant
- Obesity Treatment Device
- Implanted Urinary and Fecal Incontinence Device








General controls sufficient?
Yes
Class I
No
Sufficient info for special controls?
Yes
Class II
No
Life supporting/ sustaining/ substantially important to human health?
Yes
Class III
No
Potential unreasonable risk?
Yes
No

What is “Reasonable Assurance of Safety”?

As defined in 21 CFR 860.7(d)(1), “There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use.”

What is “Reasonable Assurance of Effectiveness”?

As defined in 21 CFR 860.7(e)(1), “There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.”

Valid Scientific Evidence

"Valid Scientific Evidence" is defined in 21 CFR 860.7(c)(2) and includes:

- Well-controlled investigations
- Partially controlled studies;
- Studies without matched controls
- Well-documented case histories; and
- Reports of significant human experience with a marketed device

from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use.

What We Need from the Panel

- Review and discuss available scientific evidence regarding safety and effectiveness of wound dressings combined with drugs.
- Input on classification of the device types
  - Class III, Class II, or Class I
- Input and recommendations should include:
  - Identify risks to health presented by the device
  - Whether the device is life-supporting/life-sustaining, of substantial importance in preventing impairment to human health, or presents a potential unreasonable risk of illness or injury
  - Whether sufficient information exists to develop special controls
  - If so, identify special controls that provide reasonable assurance of safety and effectiveness
  - Whether general controls alone are sufficient

What Will Happen After This Panel Meeting?

- FDA will consider the available evidence, including the input of this panel and the public comments
- FDA will issue a proposed rule, proposing classification of the device and seeking public comment on the proposal
- FDA will issue a final rule identifying the appropriate class
  - If Class I or Class II, devices may continue to be marketed
  - If Class III, will issue a separate call for PMAs
    - Existing devices will remain on the market until submission of a PMA by specified time to continue marketing
    - If PMA is not approved, devices will be considered misbranded and must be removed from distribution

Clarifying Questions from Panel

Classification, Risks and Mitigations

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Overview

- Scope of Classification Discussion
- Solid Dressings
  - Risks
  - Potential mitigations
- Creams/Gels/Ointments
  - Risks
  - Potential mitigations
- Liquid Wound Washes
  - Risks
  - Potential mitigations

Scope of Classification: Included

- Wound Dressings Combined with Drugs
  - Unclassified
  - Product Code FRO
    - Solid
    - Gel/Cream/Ointment
    - Liquid
  - Combined with Drugs
    - Antimicrobials
    - Other ingredients listed in Appendix 2 of Executive Summary
    - Indications for Use and Conditions of Use vary from approval/monograph

Scope of Classification: Excluded

- Interactive wound dressings (Class III):
  - Product code MGR
  - Life-supporting or life-sustaining
  - Intended to replace full function of skin
  - Promote wound healing through active interaction with wound
- Wound dressings composed of animal-derived materials (no drugs)
- Wound dressings with biologics
- Hemostatic wound dressings

Solid Wound Dressings: Composition

- Base material
  - Synthetic/naturally derived
  - Biodegradable/non-biodegradable
- Structural strength for physical form
  - Scaffold/matrix
  - Single or multiple layers
- Typically combined with antimicrobials
  - Silver, bismuth, chlorhexidine, polyhexamethylene biguanide (PHMB), and bacitracin.

Solid Wound Dressings: Indications

- Intended use
  - Cover/protect wound
  - Absorb exudate
  - Provide/support moist wound environment
- Wound types
  - Traumatic, partial thickness burns, ulcers, surgical wounds
  - Catheter insertion sites, other percutaneous device insertion sites

Solid Wound Dressings: Risks

Potential Risks to Health
• Adverse tissue reaction (e.g., toxicity, allergic reaction, irritation and sensitization) • Delays in wound healing • Incompatibilities with other therapies • Increased risk of contributing to antimicrobial resistance • Infection • Loss of barrier function • Microbial growth within the product • Product degradation during storage • Retention of dressing material in wound

Solid Wound Dressings: Mitigations

Identified Risk	Potential Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Delays in wound healing	• *In vivo* evaluation
Incompatibilities with other therapies	• Labeling
Increased risk of contributing to antimicrobial resistance	• Evaluation and identification of the risk and potential mechanisms for resistance development • Labeling
Infection	• Labeling • Shelf-life validation • Sterilization validation • Preservative effectiveness testing
Loss of barrier function	• Microbial barrier effectiveness testing • Water loss/moisture barrier effectiveness testing
Microbial growth within the product	• Antimicrobial effectiveness testing
Product degradation during shelf storage	• Labeling • Shelf-life validation
Retention of dressing material in wound	• Labeling

Gels, Creams, Ointments: Composition

- Amorphous
  - High water content with thickeners
  - Oil-water emulsions
- Typically combined with drugs
  - Antimicrobials/preservatives
  - Plant-derived materials or extracts
- Packaged in tubes or bottles
  - Single or multiple use
  - May or may not be sterilized

Gels, Creams, Ointments: Indications

- Intended use
  - Provide/support moist wound environment
    - Relieve the symptoms of skin irritations, such as dryness, itching, and pain
- Wound types
  - Traumatic, partial thickness burns, ulcers, surgical wounds
  - Skin irritations, various dermatoses
    - Radiation dermatitis
    - Seborrheic dermatitis

Gels, Creams, Ointments: Risks

Potential Risks to Health
• Adverse tissue reaction • Delays in wound healing • Incompatibilities with other therapies • Increased risk of contributing to antimicrobial resistance • Infection • Microbial growth within the product • Product degradation during shelf storage

Gels, Creams, Ointments: Mitigations

Identified Risk	Potential Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Delays in wound healing	• In vivo evaluation
Incompatibilities with other therapies	• Labeling
Increased risk of contributing to antimicrobial resistance	• Evaluation and identification of the risk and potential mechanisms for resistance development • Labeling
Infection	• Sterilization validation • Preservative effectiveness testing • Shelf-life validation • Labeling
Microbial growth within the product	• Antimicrobial effectiveness testing
Product degradation during shelf storage	• Shelf-life validation • Labeling

Liquid Wound Washes: Composition

- Liquid solutions
  - Water or saline-based
- Often combined with drugs
  - Salts/surfactants
  - Antimicrobials
    - Hypochlorous acid/sodium hypochlorite
    - Silver
    - PHMB
- Packaged in bottles with caps or pump sprays
- May or may not be sterilized

Liquid Wound Washes: Indications

- Intended use
  - Rinse or irrigate a wound
  - To remove foreign material, such as debris, microbes, and wound exudate.
- Wound types
    - Traumatic
    - Partial thickness burns
    - Ulcers
    - Surgical wounds

Liquid Wound Washes: Risks

Potential Risks to Health
• Adverse tissue reaction • Delays in wound healing • Inability to remove wound debris and foreign materials • Incompatibilities with other therapies • Increased risk of contributing to antimicrobial resistance • Infection • Microbial growth within the product • Product degradation during shelf storage

Liquid Wound Washes: Mitigations

Identified Risk	Potential Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Delays in wound healing	• *In vivo* evaluation
Loss of barrier function	• Microbial barrier effectiveness testing • Water loss/moisture barrier effectiveness testing
Inability to remove wound debris and foreign materials	• Labeling • Bench performance testing
Incompatibilities with other therapies	• Labeling
Increased risk of contributing to antimicrobial resistance	• Evaluation and identification of the risk and potential mechanisms for resistance development • Labeling
Infection	• Sterilization validation • Preservative effectiveness testing • Shelf-life validation • Labeling
Microbial growth within the product	• Antimicrobial effectiveness testing
Product degradation during shelf storage	• Shelf-life validation • Labeling

Clarifying Questions from Panel

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PANEL QUESTIONS - DAY 2

Panel Questions – Day 2

In the previous presentation, FDA described three categories of wound dressings combined with drugs:

1) Solid Wound Dressings combined with Drugs,
2) Wound Dressings combined with Drugs formulated as a Cream, Gel, or Ointment, and
3) Liquid Wound Washes combined with Drugs.

For the remainder of the day, you will be asked to address a set of questions for each of the three categories. As you respond to the following questions, please remember the definition of each wound dressing category.

Question 1

Solid Wound Dressings Combined with Drugs

For Solid Wound Dressings combined with Drugs, FDA has identified the following risks to health based upon review of: the medical literature, information available to FDA on cleared products, and the Medical Device Report databases. Please comment on whether you agree with the Potential Risks to Health presented below and identified in the overall risk assessment of these products within the product code FRO. In addition, please comment on whether any additional risks should be included in this overall risk assessment of Solid Wound Dressings combined with Drugs under the product code FRO.

Dressing Type	Potential Risks to Health
Solid wound dressings	• Adverse tissue reaction (e.g., toxicity, allergic reaction, irritation and sensitization) • Delays in wound healing • Incompatibilities with other therapies • Increased risk of contributing to antimicrobial resistance • Infection • Loss of barrier function • Microbial growth within the product • Product degradation during storage • Retention of dressing material in wound

Question 2

Solid Wound Dressings Combined with Drugs

For Solid Wound Dressings combined with Drugs, the risk/mitigation table below outlines the identified risks to health and potential regulatory controls/data requirements that FDA could apply for each identified risk. Please discuss each of these potential controls and whether it, either alone or in combination with others, adequately mitigates the identified risk(s).

Identified Risk	Potential Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Delays in wound healing	• In vivo evaluation
Incompatibilities with other therapies	• Labeling
Increased risk of contributing to antimicrobial resistance	• Evaluation and identification of the risk and potential mechanisms for resistance development • Labeling
Infection	• Labeling • Shelf-life validation • Sterilization validation • Preservative effectiveness testing
Loss of barrier function	• Microbial barrier effectiveness testing • Water loss/moisture barrier effectiveness testing
Microbial growth within the product	• Antimicrobial effectiveness testing
Product degradation during shelf storage	• Labeling • Shelf-life validation
Retention of dressing material in wound	• Labeling

Solid Wound Dressings Combined with Drugs

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

- insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness AND insufficient information exists to determine that application of special controls would provide such assurance, AND
- the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or 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.

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
    - the device 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
    - it does not present a potential unreasonable risk of illness or injury.

Question 3

Solid Wound Dressings Combined with Drugs

FDA believes that general controls, by themselves, are insufficient to provide a reasonable assurance of product safety and effectiveness. For Solid Wound Dressings combined with Drugs please comment on whether:

a. sufficient information exists to establish special controls to adequately mitigate the risks to health and provide a reasonable assurance of device safety and effectiveness for this device type;

b. the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or the device presents a potential unreasonable risk of illness or injury.

Solid Wound Dressings Combined with Drugs

For the category of Solid Wound Dressings combined with Drugs, please provide a recommendation regarding which products should be classified into Class II or into Class III? Please discuss the reasons for your recommendation.

Question 4

Wound Dressings Combined with Drugs Formulated as a Cream, Gel, or Ointment

For Wound Dressings combined with Drugs formulated as a Cream, Gel, or Ointment, FDA has identified the following risks to health based upon review of: the medical literature, information available to FDA on cleared products, and the Medical Device Report databases. Please comment on whether you agree with the Potential Risks to Health presented below and identified in the overall risk assessment of these products within the product code FRO. In addition, please comment on whether any additional risks should be included in this overall risk assessment of a Wound Dressing combined with Drugs formulated as a Cream, Gel, or Ointment under the product code FRO.

Dressing Type	Potential Risks to Health
Creams, gels, ointments	• Adverse tissue reaction • Delays in wound healing • Incompatibilities with other therapies • Increased risk of contributing to antimicrobial resistance • Infection • Microbial growth within the product • Product degradation during shelf storage

Question 5

Wound Dressings Combined with Drugs Formulated as a Cream, Gel, or Ointment

For Wound Dressings combined with Drugs formulated as a Cream, Gel, or Ointment, the risk/mitigation table below outlines the identified risks to health and potential regulatory controls/data requirements that FDA could apply for each identified risk. Please discuss each of these potential controls and whether it, either alone or in combination with others, adequately mitigates the identified risk(s).

Identified Risk	Potential Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Delays in wound healing	• *In vivo* evaluation
Incompatibilities with other therapies	• Labeling
Increased risk of contributing to antimicrobial resistance	• Evaluation and identification of the risk and potential mechanisms for resistance development • Labeling
Infection	• Sterilization validation • Preservative effectiveness testing • Shelf-life validation • Labeling
Microbial growth within the product	• Antimicrobial effectiveness testing
Product degradation during shelf storage	• Shelf-life validation • Labeling

Question 6

Wound Dressings Combined with Drugs Formulated as a Cream, Gel, or Ointment

Consistent with Section 513 of the FD&C Act, please consider the following:

a. FDA believes that general controls, by themselves, are insufficient to provide a reasonable assurance of product safety and effectiveness. For Wound Dressings combined with Drugs formulated as a Cream, Gel, or Ointment, please comment on whether:

   i. sufficient information exists to establish special controls to adequately mitigate the risks to health and provide a reasonable assurance of device safety and effectiveness for this device type;

   ii. the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or the device presents a potential unreasonable risk of illness or injury.

b. For the category of Wound Dressings combined with Drugs formulated as a Cream, Gel, or Ointment, please provide a recommendation regarding which products should be classified into Class II or into III? Please discuss the reasons for your recommendation

Question 7

Liquid Wound Washes Combined with Drugs

For Liquid Wound Washes combined with Drugs, FDA has identified the following risks to health based upon review of: the medical literature, information available to FDA on cleared products, and the Medical Device Report databases. Please comment on whether you agree with the Potential Risks to Health presented below and identified in the overall risk assessment of these products within the product code FRO. In addition, please comment on whether any additional risks should be included in this overall risk assessment of Liquid Wound Washes combined with Drugs under the product code FRO.

Dressing Type	Potential Risks to Health
Liquid wound washes	• Adverse tissue reaction • Delays in wound healing • Inability to remove wound debris and foreign materials • Incompatibilities with other therapies • Increased risk of contributing to antimicrobial resistance • Infection • Microbial growth within product • Product degradation during shelf storage

Question 8

Liquid Wound Washes Combined with Drugs

For Liquid Wound Washes combined with Drugs, the risk/mitigation table below outlines the identified risks to health and potential regulatory controls/data requirements that FDA could apply for each identified risk. Please discuss each of these potential controls and whether it, either alone or in combination with others, adequately mitigates the identified risk(s).

Identified Risk	Potential Mitigation Measure
Adverse tissue reaction	• Biocompatibility evaluation
Delays in wound healing	• *In vivo* evaluation
Loss of barrier function	• Microbial barrier effectiveness testing • Water loss/moisture barrier effectiveness testing
Inability to remove wound debris and foreign materials	• Labeling • Bench performance testing
Incompatibilities with other therapies	• Labeling
Increased risk of contributing to antimicrobial resistance	• Evaluation and identification of the risk and potential mechanisms for resistance development • Labeling
Infection	• Sterilization validation • Preservative effectiveness testing • Shelf-life validation • Labeling
Microbial growth within the product	• Antimicrobial effectiveness testing
Product degradation during shelf storage	• Shelf-life validation • Labeling

Question 9

Liquid Wound Washes Combined with Drugs

Consistent with Section 513 of the FD&C Act, please consider the following:

a. FDA believes that general controls, by themselves, are insufficient to provide a reasonable assurance of product safety and effectiveness. For Liquid Wound Washes combined with Drugs please comment on whether:

   i. sufficient information exists to establish special controls to adequately mitigate the risks to health and provide a reasonable assurance of device safety and effectiveness for this device type;

   ii. the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or the device presents a potential unreasonable risk of illness or injury.

b. For the category of Liquid Wound Washes combined with Drugs, please provide a recommendation regarding which products should be classified into Class II or into Class III? Please discuss the reasons for your recommendation.


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