U.S. FOOD & DRUG ADMINISTRATION

Welcome To Today's Webinar

Thanks for joining us!
We'll get started in a few minutes

Today's Topic:
Biocompatibility Guidance Update: Certain Devices in Contact with Intact Skin

October 12, 2023

Biocompatibility Guidance Update: Certain Devices in Contact with Intact Skin

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Final Guidance

- **Attachment G: Biocompatibility of Certain Devices in Contact with Intact Skin in the Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process", issued on September 8, 2023**
  - www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and

Learning Objectives

- Describe purpose of this FDA Biocompatibility Guidance update
- Identify devices, components and materials included in and excluded from this update
- Describe information and labeling needed for a premarket submission
- Describe changes made to electronic Submission Template and Resource (eSTAR) form
- Describe additional minor revisions to guidance to match the current recognized versions of relevant consensus standards

Purpose of Guidance Update

Background

- Many devices have intact skin contacting materials made from synthetic polymers and natural fabrics
- These materials pose a very low biocompatibility risk because they have a long history of safe use in legally marketed medical devices that contact intact skin
- Attachment G describes a least burdensome approach for these devices that recommends specific material information to be included in a premarket submission in lieu of biocompatibility testing
- This approach supports the principles of the “3Rs,” to replace, reduce, and/or refine animal use in testing when feasible

Included Devices, Components, and Materials

Which Types of Devices Are Included? (Section A)

Devices that meet **all** of the following characteristics:

- Medical devices or components that contact intact skin surfaces only, as described in section 5.2.2 (a) of International Standards Organization (ISO) 10993-1:2018: Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process
  - EXAMPLE: Does **NOT** include mucous membranes or open or healing wounds
- Limited (≤24 hour), prolonged (>24 hours to 30 days), and long term (>30 days) durations of contact, including repeat use devices, AND
- Composed of a single material or multiple materials outlined in Section B of Attachment G

What Materials Are Included?
(Section B)

Synthetic Polymers	
Acrylonitrile-butadiene-styrene plastic (ABS)	Polychloroprene, such as neoprene
Cellulose Acetate	Polyetheretherketone (PEEK)
Cured epoxy adhesives	Polyetherketoneketone (PEKK)
Fluoropolymers, including PTFE, ePTFE, PVDF, FEP	Polyether block amide (PEBA), such as PEBAX®
Nitrile Butadiene Rubber (NBR)	Polyether imide (PEI)
Parylene	Polyethylenes, including LDPE and HDPE
Polyamides (PA), such as nylon and Velcro®	Poly(ethylene terephthalate) (PET), such as Velcro®
Poly(butylene terephthalate) (PBT)	Poly(methyl methacrylate) (PMMA)
Polycarbonate (PC)	Polyoxymethylene (POM)

What Materials Are Included?
(Section B)

Synthetic Polymers (Cont.)	
Poly(phenylene sulfone) (PPSU)	Polyurethanes (PUR), such as Lycra®
Polypropylene (PP)	Polyvinyl alcohol (PVA)
Polystyrene (PS), including HIPS	Silicone

Natural Fabrics	
Cotton fabrics	Silk fabrics
Rayon fabrics	

Examples: Devices and Components

Example 1

- Device Type: Biomicroscope
- Regulation: 21 CFR 886.1850
- Product Code: HJO
- Description: Device used in the ophthalmologist office for microscopic assessments of your eye
- Intact Skin Contacting Components: Head rest, chin rest

CFR = Code of Federal Regulations

Examples: Devices and Components

Example 2

- Device Type: Oximeter
- Regulation: 21 CFR 870.2700
- Product Code: DQA
- Description: Small device that slides over your fingertip to measure your blood oxygen levels
- Intact Skin Contacting Components: Finger cushion, external case and interactive components

Examples: Devices and Components

Example 3

- Device Type: Blood Pressure Cuff
- Regulation: 21 CFR 870.1120
- Product Code: DXQ
- Description: Inflatable sleeve wrapped around your arm for measuring your blood pressure by another device
- Intact Skin Contacting Component: Entire device

Examples: Devices and Components

Example 4

- Device Type: Powered Inflatable Tube Massager
- Regulation: 21 CFR 890.5650
- Product Code: IRP
- Description: Device that uses air compression to help relieve minor muscle aches and pains and to increase circulation of your legs
- Intact Skin Contacting Components: Leg wraps

Situations to Discuss in a Q-Submission

- If legally marketed device* made from same material:
  - Was found to be toxic in previous testing, OR
  - Resulted in adverse clinical findings after marketing that may be related to cytotoxicity, irritation, or sensitization, such as:
    - Redness (erythema), swelling (edema), allergy, and immune response or other reactions on the skin where the device has contact

*For the purposes of this guidance, “legally marketed devices” are limited to devices marketed in the U.S.

Situations to Discuss in a Q-Submission

- If proposed device is:
  - Indicated for use with neonates,
  - Indicated for use in pregnant women, OR
  - A device-led combination product, or a device comprised of biologically-derived material, such as tissues derived from animal or plant material

Excluded Devices, Components, and Materials

Which Types of Devices Are Excluded? (Section C)

Medical Device Characteristic	Reason for exclusion
Intact skin contacting components fabricated from materials that are not explicitly included in the above list, including novel materials and bulk metals, such as titanium, stainless steel, nickel, nitinol, gold, cobalt, chrome	• These materials may introduce toxicity risks
Stored in or containing fluids or creams	• Increased risk that leachables can be transferred into the fluid or cream and then absorbed through the skin
Fabricated from in-situ polymerizing materials, absorbable materials, or hydrogels	• Increased risk that polymerization or degradation products can change over time. • Manufacturing process can impact the type and quantity of intermediate and final chemicals, which could introduce a toxicity risk

Which Types of Devices Are Excluded?

(Section C)

Medical Device Characteristic	Reason for exclusion
Contacts breached or compromised surfaces, such as open or healing wounds	• Increased risk that leachables can be transferred through breached or compromised skin
Reprocessed single-use devices	• Reprocessing can cause adverse biological responses, such as irritation
Adhesives used to attach a device directly to the skin, such as electrode pads, on-body pump attachment systems	• Can cause adverse biological responses, such as irritation

Information and Labeling for a Premarket Submission

Biocompatibility Information Needed (Section D)

1. **For all premarket submissions (PMA, HDE, IDE, 510(k), De Novo):**
   - List all materials (including color additives) used to fabricate device or component with only direct or indirect skin contact;
   - Provide statement confirming that device materials are listed in Section B, and have a documented history of safe use in legally marketed medical devices in contact with intact skin, such as through Medical Device Reporting (MDR) analysis, literature search; and
   - Provide statement confirming that none of exclusions listed in Section C apply.

PMA = Premarket Approval Application
HDE = Humanitarian Device Exemption
IDE = Investigational Device Exemption

Biocompatibility Information Needed (Section D)

2. Additional recommendations for IDE applications:

- Discuss any adverse biological responses from devices within this intact skin policy in IDE progress reports submitted pursuant to 21 CFR 812.150(b)(5).
- Specifically describe any redness (erythema), swelling (edema), irritation, sensitization (delayed Type IV hypersensitivity), allergy, immune response, or other reactions observed by investigators during course of a clinical study with observations attributed to a specific device, if relevant.

Biocompatibility Information Needed (Section D)

3. **Additional recommendations for marketing submissions (PMA, HDE, 510(k), De Novo):**
   - Include a statement that the manufacturer has documented in their Device Master Record (DMR) how they have determined that biocompatibility risks for their device are addressed such that biocompatibility testing, and a detailed rationale regarding manufacturing, is not necessary to include in a premarket submission.

Biocompatibility Information Needed (Section D)

Example Statement:

"We have documented in the Device Master Record (DMR) that we have addressed any concerns that have been identified through biocompatibility testing (i.e., cytotoxicity, irritation, and sensitization), manufacturing information (based on the type of materials, formulation (if available) and nature of contact) and/or relevant quality system requirements and postmarket controls related to:

- Purchasing controls (21 CFR 820.50) of device materials,
- Production and process controls (21 CFR 820.70) for manufacturing materials,
- Acceptance activities (21 CFR 820.80) for component and manufacturing materials,
- Corrective and preventative action (21 CFR 820.100),
- Complaint files (21 CFR 820.198), and
- Medical device reporting (MDR) (21 CFR 803)."

Certain Labeling Information
(Section E)

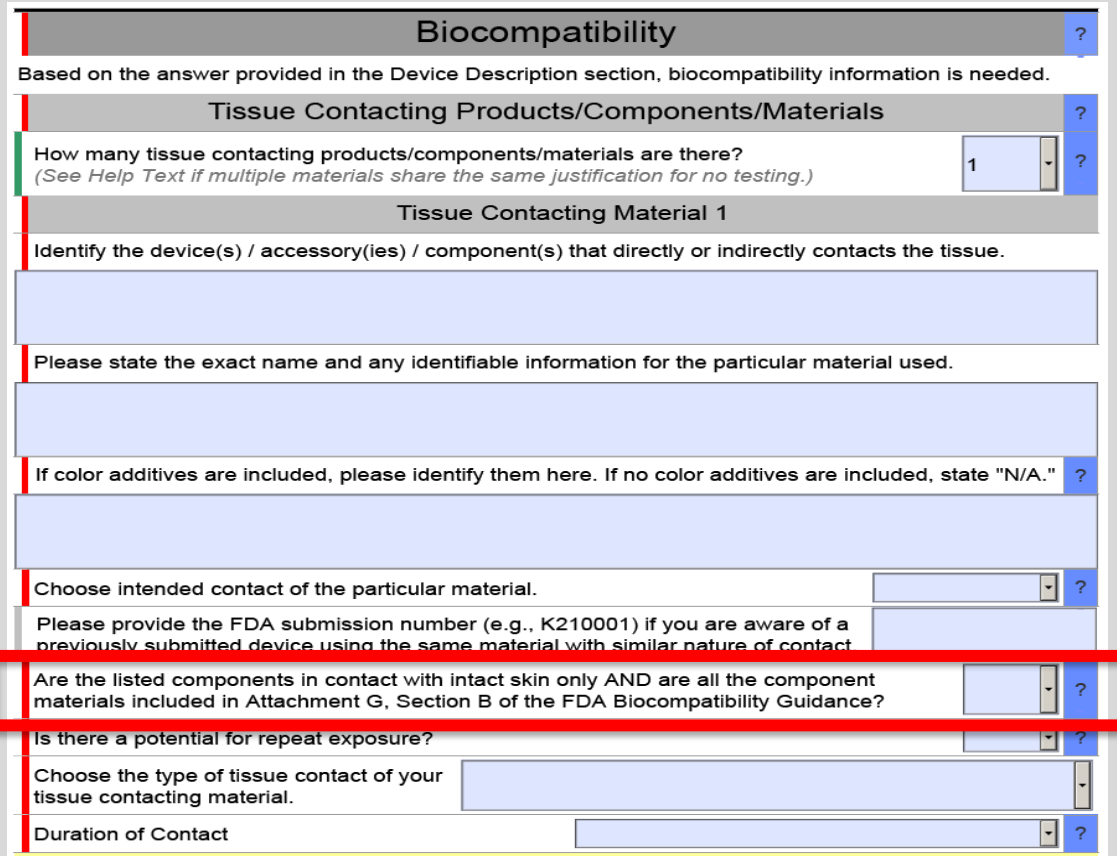
- When device is intended for use in a patient population that may not have the ability to identify adverse biological reactions related to cytotoxicity, irritation, or sensitization, such as patients with epilepsy or dementia, or the vision impaired
- FDA recommends that manufacturers inform caretakers in labeling by including a precaution discussing common adverse skin reactions

Example Statement:

"Caretakers should assess patients for adverse reactions on the skin where the device has contact, such as redness (erythema), swelling (edema), irritation, sensitization (delayed Type IV hypersensitivity), allergy, immune response, or other reactions."

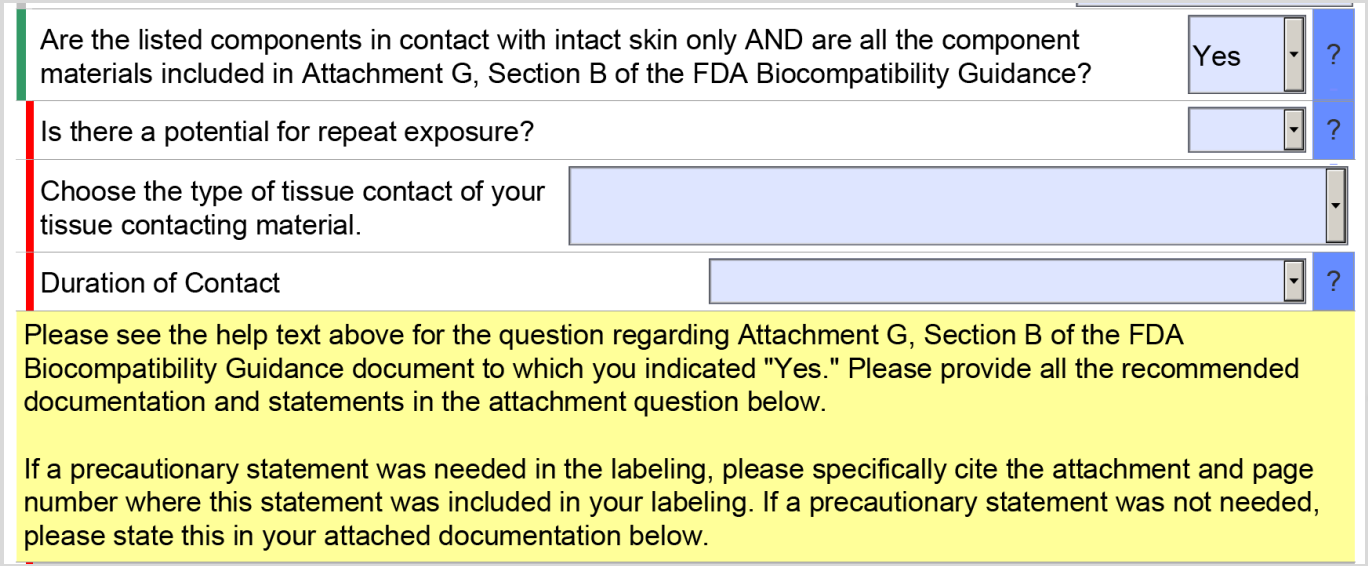
Revisions in eSTAR Form

eSTAR Changes



Newly Added

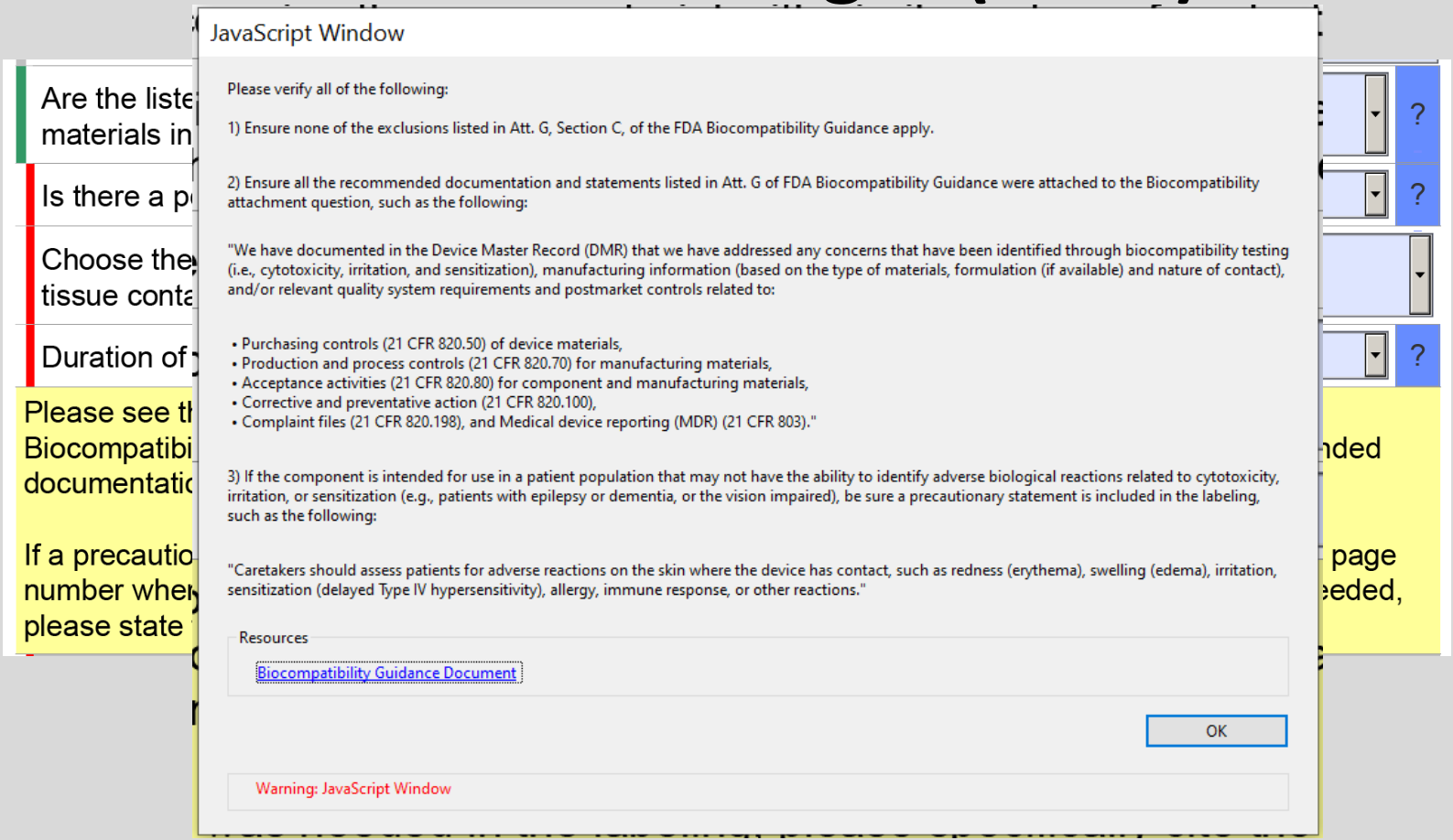
eSTAR Changes (cont.)



Click to open

Intact skin specific instructions

eSTAR Changes (cont.)



Some Additional Revisions

Some Additional Revisions

- Minor revisions for clarity and consistency within guidance and with currently recognized versions of consensus standards
- Update of links in footnotes, including currently recognized consensus standards and FDA guidances
- Inclusion of language about Accreditation Scheme for Conformity Assessment (ASCA) Program
- Update on recommendations about studies not in compliance with the FDA Good Laboratory Practice Regulations
- Attachment A: Updated to be consistent with recommendations in ISO 10993-1:2018

Additional Resource

- Biocompatibility Assessment Resource Center
  - www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/biocompatibility-assessment-resource-center

Summary

- Some synthetic polymers and natural fabrics pose a very low biocompatibility risk
  - because they have a long history of safe use in legally marketed medical devices that contact intact skin
- Attachment G of updated guidance includes a least burdensome approach for certain devices or components in contact with intact skin
  - that allows sponsors to include specific material information and certain labeling information in a premarket submission in lieu of biocompatibility testing or rationales
- eSTAR form has been updated to include this policy
- Minor revisions have been made to the main Biocompatibility Guidance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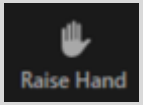
Let's Take Your Questions

- **To Ask a Question:**
  1. Raise your hand in Zoom 

  2. Moderator will announce your name and invite you to ask your question
  3. Unmute yourself when prompted in Zoom to ask your question

- **When Asking a Question:**
  - Ask one question only
  - Keep question short
  - No questions about specific submissions

- **After Question is Answered:**
  - Mute yourself and lower your hand
  - If you have more questions - raise your hand again

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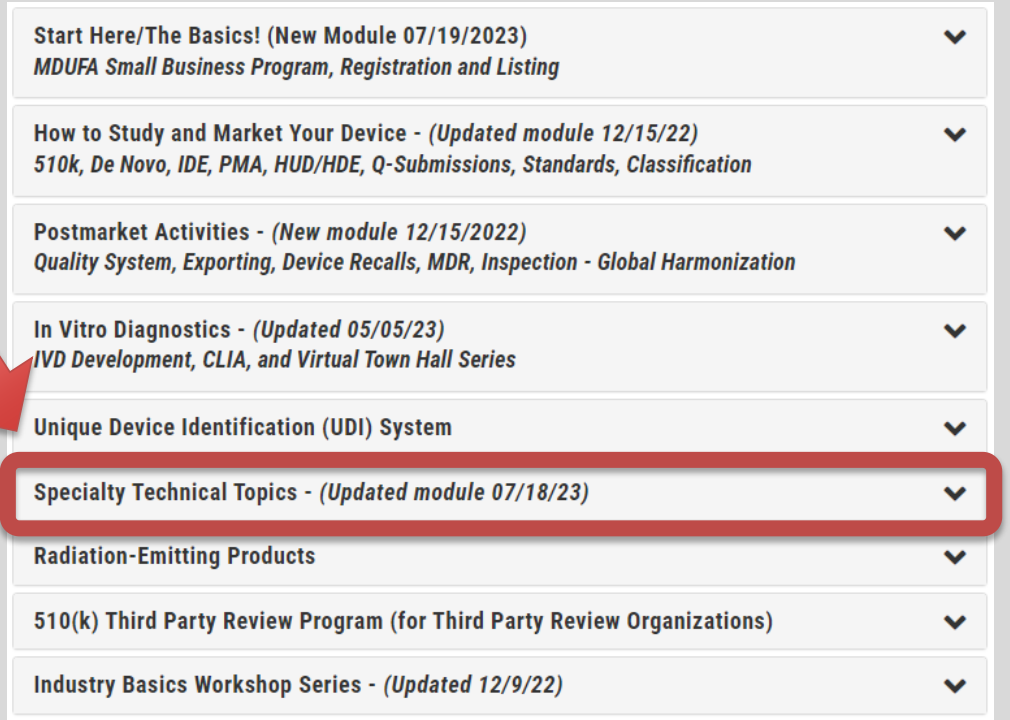


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