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Conveying Materials Information about Medical Devices to Patients and Healthcare Providers: Considerations for a Framework.

Center for Devices and Radiological Health

Conveying Materials Information about Medical Devices to Patients and Healthcare Providers: Considerations for a Framework

Discussion Paper and Request for Feedback

This discussion paper is intended for discussion purposes only and does not represent draft or final guidance. It is not intended to propose or implement policy changes regarding labeling of medical devices or the applicable statutory and regulatory requirements for entities conducting these activities or submitting information to the FDA. This document is not intended to communicate the FDA's proposed (or final) regulatory expectations but is instead meant to seek early input from groups and individuals outside the Agency.

The objective of this discussion paper is to obtain public comment and additional stakeholder feedback on a series of questions related to the inclusion of specific materials information in medical device labeling that may be helpful for patients and healthcare providers to make informed decisions regarding medical device use. Please submit your comments regarding this discussion paper to https://www.regulations.gov, Docket No. FDA-2021-N-0334 within 60 days. FDA will consider all comments submitted to this docket (FDA-2021- N-0334) before issuing subsequent documents or draft guidance related to this topic.

I. Introduction

The Center for Devices and Radiological Health (CDRH) is committed to ensuring that patients and healthcare providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products. The safety of materials from which certain devices are manufactured or processed has generated substantial interest from stakeholders who want to be better informed regarding medical device materials and their impact on the benefits and risks of medical devices. The objective of this discussion paper is to provide an initial framework to stimulate discussion and to solicit feedback from a variety of stakeholders on how materials information could be communicated. The current discussion paper provides an initial framework to aid in this goal and includes examples of how comprehensive information on materials used in devices with long-term exposure (not only information limited to only those materials with currently known health concerns) could be communicated so that patients and healthcare providers may make better informed benefit-risk decisions regarding the use of medical devices. For the purposes of this document, CDRH has defined "long term exposure" as medical devices whose cumulative sum of single, multiple or repeated contact time exceeds 30 days as described in section 5.3(c) of ISO 10993-1:2018 Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing Within a Risk Management Process.[1]

[1] ISO 10993-1:2018 Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing Within a Risk Management Process, https://www.iso.org/standard/68936.html.

II. Background

In recent years, several high-profile safety concerns associated with certain medical devices with long-term exposure such as female sterilization devices,[2] metal on metal hips,[3] and breast implants[4] have emerged. In each of these cases, there has been discussion in the stakeholder community of the materials utilized in these medical devices and their potential association with adverse events being reported to FDA. In announcements in March and September 2019, FDA noted that it was seeking public input to better understand how a patient responds to materials used in medical device implants and to improve the safety of devices in patients.[5]

As a part of our strategy, CDRH completed a scientific literature review[6] of metal-containing implants regulated as medical devices and held a public meeting of the Immunology Devices Panel of the Medical Devices Advisory Committee (2019 Immunology Devices Panel) to discuss immunological responses to metal-containing implants (November 13-14, 2019).[7] In the open public hearing of the 2019 Immunology Devices Panel, patients, healthcare providers, and industry representatives all noted the desire to have additional information on the materials of implantable devices so that patients and healthcare providers can make informed decisions regarding device use. This was echoed by the panel members, who agreed it is important and beneficial for patient safety to have the device packaging and labeling include a list of the elemental composition of the device.[8]

While the 2019 Immunology Devices Panel was specifically focused on metal containing implants, CDRH has envisioned a broader approach to materials safety and evaluation, so as not to limit such evaluation to a single type of material. For example, FDA's recent guidance on breast implant materials[9] recommends the listing of multiple types of materials. This current discussion paper is intended to stimulate discussion on CDRH's broader approach with respect to medical devices with long term exposure to improve informed decision-making through transparency about materials in such devices to which an individual may have had or could develop an immunological response resulting in adverse

[2] See the FDA website on Essure at https://www.fda.gov/medical-devices/implants-and-prosthetics/essure-permanent-birth-control.
[3] See the FDA website on metal-on-metal hips at https://www.fda.gov/medical-devices/implants-and-prosthetics/metal-metal-hip-implants.
[4] See the FDA website on breast implants at https://www.fda.gov/medical-devices/implants-and-prosthetics/breast-implants.
[5] See the March 15, and September 30, 2019 Statements at https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-jeff-shuren-md-director-center-devices-and-3 and at https://www.fda.gov/news-events/press-announcements/statement-continued-efforts-evaluate-materials-medical-devices-address-potential-safety-questions.
[6] See full review on FDA's website at https://www.fda.gov/media/131150/download.
[7] See the November 13-14, 2019 Immunology Devices Panel of the Medical Devices Advisory Committee Meeting materials at https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-13-14-2019-immunology-devices-panel-medical-devices-advisory-committee-meeting-announcement.
[8] See the full transcript of the meeting on FDA's website at https://www.fda.gov/media/133730/download.
[9] See the Breast Implants - Certain Labeling Recommendations to Improve Patient Communication, *Guidance for Industry and Food and Drug Administration Staff*, (SEPTEMBER 2020) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breast-implants-certain-labeling-recommendations-improve-patient-communication.

health consequences. Providing such information to patients and providers could allow them to make better informed decisions about which medical devices may or may not be most appropriate for an individual patient, and facilitate identifying whether an immunologic/hypersensitivity response to a material in a device was the cause of adverse health consequences experienced by the patient in whom the device was used.

Labeling requirements for medical devices were established in the Federal Food, Drug, and Cosmetic Act (FD&C Act), and in the implementing regulations.[10] Labeling for medical devices may include various labels and other written, printed, or graphic matter, including documents, but the most prevalent are the healthcare provider labeling and patient labeling. Healthcare provider labeling serves an important role to ensure the healthcare provider has specific information about the device, including conditions of use, effects, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and warnings and precautions under which the device can safely be used. Patient labeling,[11] which is targeted to the patient or lay caregiver, may also serve a critical role in contributing to safe and effective use of a medical device by, for example: assisting the end user in understanding the device; describing the way it interacts with the body to accomplish its purpose; providing benefit-risk information; including recommendations for its safe operation, care, maintenance, and if applicable, disposal. Some examples of currently available patient labeling include patient brochures or implant cards (e.g., for MRI compatibility), however not all devices with long term exposure (> 30-day) currently have patient labeling.[12,13]

Given the importance of labeling, which is intended to provide patients and healthcare providers appropriate access to information on the materials of devices with long-term exposure, CDRH believes that promoting greater clarity, predictability and consistency in the content and format of medical device labeling with respect to constituent materials could allow providers and patients to make better informed decisions about whether or not to use a particular device. It may also help identify whether adverse health consequences an individual experienced could have been due to an immunologic/hypersensitivity response to material contained in a device.

CDRH believes that the development of a framework with sufficient flexibility to consider the inclusion of additional information regarding materials in labeling for certain medical devices could be beneficial and promote transparency to stakeholders. Therefore, CDRH is looking to solicit stakeholder input on

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[10] See the FDA website on Device Labeling at https://www.fda.gov/medical-devices/overview-device-regulation/device-labeling.

[11] See Guidance on Medical Device Patient Labeling, *Final Guidance for Industry and FDA Staff*, (APRIL 2001), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-medical-device-patient-labeling.

[12] See Breast Implants - Certain Labeling Recommendations to Improve Patient Communication, *Guidance for Industry and Food and Drug Administration Staff* (SEPTEMBER 2020), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breast-implants-certain-labeling-recommendations-improve-patient-communication.

[13] See Technical Considerations for Non-Clinical Assessment of Medical Devices Containing Nitinol, *Guidance for Industry and Food and Drug Administration Staff* (OCTOBER 2020), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-non-clinical-assessment-medical-devices-containing-nitinol.

the best approaches to provide specific materials information for medical devices to reflect a risk-based and least burdensome approach[14]. CDRH is also aiming to ensure that information, which may be critical as well as helpful for patients and healthcare providers to make informed benefit-risk decisions regarding medical device use, is made available, accessible, and understandable.

III. Points of Discussion

CDRH is currently seeking stakeholder feedback on the consideration to include more specific materials information on patient-contacting materials in labeling for devices with long-term exposure (*see Appendix A and B for hypothetical examples*). Devices for consideration and for which comments are sought may include medical devices that are implanted or are intended to be utilized repeatedly for a duration totaling greater than 30 days.

CDRH has initially considered several factors we believe are important for providing relevant materials information in labeling to allow patients and healthcare providers to be adequately informed in making decisions regarding medical device use:

- Duration of implantation. Many implants are not intended to be removed. Devices that are not intended to be removed may pose additional risks should they require removal (e.g., additional surgical procedures and complications resulting from removal). In these situations, inclusion of the specific materials and/or constituents of the materials may be informative and relevant to stakeholders.
- Duration of contact. Although not always the case, generally, devices with longer duration or repeated contact may pose a greater risk of eliciting an adverse reaction as compared to devices with more limited contact duration (e.g., less than 30 days).
- Usefulness of labeling. Ideally, specific materials information included within labeling would be readily usable and understandable by stakeholders to inform decision-making.
- Diversity of devices. There are a wide diversity of medical devices, which includes many low risk devices for which it may not be necessary or appropriate to provide specific materials information in the labeling. As such, CDRH does not think it is practical or least burdensome for manufacturers to provide labeling that includes specific materials information for all devices, regardless of risk.

CDRH believes that materials information would ideally be available and presented in a manner that is consistent and easy for patients and healthcare providers to access and understand.[15,16] CDRH has initially provided a proposed format of materials listings (*examples provided in Appendix A and B of this*

[14] See The Least Burdensome Provisions: Concept and Principles, *Guidance for Industry and FDA Staff* (FEBRUARY 2019), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.
[15] See the FDA website on Device Labeling at https://www.fda.gov/medical-devices/overview-device-regulation/device-labeling.
[16] See Guidance on Medical Device Patient Labeling, *Final Guidance for Industry and FDA Staff* (APRIL 2001), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-medical-device-patient-labeling.

Discussion document) to facilitate discussion, and is requesting feedback and suggestions on how such information could be conveyed to both patients and healthcare providers.

CDRH is requesting specific feedback on the materials information conveyed in different aspects of the labeling for a medical device, including:

- Healthcare Provider Labeling
- Patient Labeling
- Format of materials information (*examples of a materials listing provided in Appendix A and B of this Discussion document*)

A listing of specific questions to stakeholders for which CDRH is requesting feedback is provided in Section V of this discussion paper.

A. Healthcare Provider Labeling

In addition to considering the inclusion of specific information on the material composition of a medical device in healthcare provider labeling, CDRH is seeking stakeholder feedback on whether healthcare provider labeling would ideally include recommendations on the counseling of patients, e.g., to expressly discuss the materials of the device with the patient prior to the procedure or implantation to further support informed decision-making. Additionally, for devices intended only for healthcare provider use (i.e., there is no patient use/contact), such as surgical masks or certain other personal protective equipment, input is being sought on information in the labeling that might be helpful to these users.

B. Patient Labeling

CDRH is seeking stakeholder feedback on the consideration that devices in contact with a patient for more than 30 days include patient labeling. Specifically, CDRH is seeking feedback on whether this consideration appropriately balances mitigation of risks with least burdensome principles[17]. In addition, CDRH is seeking feedback on the consideration that patient labeling include, along with other important information, a basic description of the device and a listing of patient-contacting materials of the device in a manner that is easily understood.

C. Materials Information (Listing)

CDRH is seeking feedback on how information on materials could be provided in labeling for devices with long term exposure (>30 days of contact). To facilitate a more robust and specific discussion, and to solicit feedback on how various materials might be described, CDRH has provided examples of materials listings with considerations for various types of materials.

CDRH understands there is a great level of complexity and variety in device design. Examples provided in this document attempt to address some of the issues that might arise in different cases; however,

[17] See The Least Burdensome Provisions: Concept and Principles, *Guidance for Industry and FDA Staff* (FEBRUARY 2019) , https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.

CDRH is seeking feedback on how various device and material-related differences might be considered in materials information provided in labeling. As adverse reactions can occur in response to a range of material types, CDRH is seeking stakeholder feedback on the consideration that all materials that could reasonably be bioavailable be listed in the healthcare provider and patient labeling for devices with long term exposure (>30 days of contact) to healthcare provider and/or patient tissue. For example, some devices might include internal components (e.g., electronics) that have known toxicities, but it is not expected to be useful to list these materials because there is no reasonable anticipation of tissue contact with these internal components. Further, devices could be designed to prevent tissue exposure to the materials from which internal components are made by employing design features such as encasement or coating.

CDRH is seeking stakeholder feedback on the consideration to use a risk-based approach to evaluate the potential for exposure. To this end, CDRH has considered in its examples, testing conducted to assess coating delamination, or component release or failure, that could expose the biological system to leaching of different chemicals, or to an increased level of chemicals from a substrate material. However, CDRH welcomes feedback on any additional considerations.

As different materials (e.g., metals, ceramics, and polymers) typically have different naming conventions and considerations, each material type is discussed separately below. To help facilitate discussion, examples of materials listings for various material types are provided in Appendices A and B. CDRH is seeking stakeholder feedback on important factors to consider for various materials when describing them in a materials listing.

(1) Metals

Metals are "a class of substances characterized by high electrical and thermal conductivity as well as by malleability, ductility, and high reflectivity of light."[18] Adverse reactions may occur in response to specific metal(s), either alone (e.g., nickel) or when incorporated in alloys (e.g., nitinol). Listing an alloy name or alloy specification alone may not provide the patient or the healthcare provider with the specific information to properly identify the potential for an allergic or other immune response to the metals in the device.

a. Possible Naming Convention

   To promote transparency and reader comprehension, specific elemental metal names (e.g., gold) rather than just the chemical symbols (e.g., Au) may be most informative. Another consideration is to list specific elemental names in descending order of predominance in the alloy.

b. Other Labeling Considerations

   Consensus standards for metal alloys often have specifications that allow for a small mass percentage of other elements to be present. Therefore, for metal alloys, the name of the

[18] https://www.britannica.com/science/metal-chemistry.

standard specification and all elements that have a minimum specification for that alloy could be listed in the labeling. If there is no standard specification for the alloy, all non-trace elements expected in the alloy could be listed in the labeling.

(2) Polymers

Polymers are "a class of natural or synthetic substances composed of very large molecules, called macromolecules, that are multiples of simpler chemical units called monomers."[19]

a. Possible Naming Convention

To promote transparency and reader comprehension, both the trade name and chemical name (e.g., monomer, copolymer, or polymer blend) may be the most informative way to communicate about polymer materials, as trade names may be the most recognizable to the lay population, and the chemical name would allow for a more thorough understanding of the specific chemicals present. If the polymer includes a color additive (at any concentration), the color additive name could be listed using the naming convention in Summary of Color Additives for Use in the United States in Food, Drugs, Cosmetics, and Medical Devices.[20]

b. Other Labeling Considerations

If there is a constituent with known toxicological risks (e.g., residual catalyst, monomer, impurity), or specific toxicological risks are identified for constituent chemicals as part of nonclinical evaluations, inclusion of additional specificity in the labeling, beyond trade name and chemical name, may allow users to make better informed benefit-risk decisions.

Similarly, it may be appropriate for some devices to include additional information on polymer composition, as described in available device-specific guidance, FDA recognized consensus standards, or based on risks identified during nonclinical evaluations. Such transparency in the form of more specific information included in the labeling may allow users to make better informed benefit-risk decisions.

Some products where additional compositional information may be informative to the end user include, but are not limited to, over-the-counter devices where compositional information may be helpful in user decision-making (e.g., personal lubricants); devices where small changes in composition could significantly impact safety and effectiveness (e.g., *in situ* polymerizing or degradable materials); or implants where specific safety risks based on common compositional constituents have been identified (e.g., metal on metal hips).[21]

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[19] www.britannica.com/science/polymer.

[20] Available at https://www.fda.gov/industry/color-additive-inventories/summary-color-additives-use-united-states-foods-drugs-cosmetics-and-medical-devices.

[21] Please see FDA's webpage on metal-on-metal hips at https://www.fda.gov/medical-devices/implants-and-prosthetics/metal-metal-hip-implants.

(3) Ceramics

Ceramics are "broadly defined as inorganic, nonmetallic materials that exhibit such useful properties as high strength and hardness, high melting temperatures, chemical inertness, and low thermal and electrical conductivity but that also display brittleness and sensitivity to flaws."[22] While ceramics often have metallic constituents, the bioavailability of metal in ceramics is much lower than in bulk metals. To differentiate between the risks associated with ceramics and metals, different naming conventions may be the most effective way to communicate this information.

a. Possible Naming Convention

To promote transparency and reader comprehension, specific elemental oxide/nitride/carbide names, rather than the chemical symbols or the common names for ceramics, could be listed in order of predominance in the ceramic.

(4) Naturally-Derived Materials: Animal Sources

Animal-derived materials used in medical devices, such as collagen, are obtained from different animal sources including cow, pig, and sheep, and come from different tissues including skin and other organs. Collagen is the most abundant animal-derived material used in medical devices. The physical and chemical properties of collagen can be affected by the composition and manufacturing methods used to purify and process collagen preparations.

a. Possible Naming Convention

To promote transparency and reader comprehension, the animal species and tissue type could be important for inclusion in the name of animal-derived materials, e.g., pig skin collagen.

b. Other Labeling Considerations

To promote transparency and reader comprehension, the predominant type or types of animal-derived material is important for consideration in the materials listing. Animal-derived materials such as collagen often contain other types of proteins and molecules that co-purify during processing; however, it may be most informative to limit information to only the constituent intended to be in the material, unless the constituent poses toxicity risks. Purity (i.e., the relative freedom from extraneous matter) is important for these products, and it could be helpful to include in the labeling the chemical names of the processing reagents such as cross-linkers. In addition, safe limits for chemicals that pose toxicity risks such as heavy metals and endotoxins could be important to include. It may be appropriate for some devices to include additional information in a naturally-derived materials listing, as described in available device-specific guidance,[23] FDA recognized consensus standards, or based on risks identified during nonclinical evaluations, similar to the scenario described in the polymer section above.

[22] https://www.britannica.com/technology/ceramics.

[23] As an example, please see device-specific guidance document "Guidance Document for Dura Substitute Devices; Guidance for Industry," issued November 9, 2000.

(5) Naturally-Derived Materials: Non-Animal Sources

Other types of naturally-derived materials (e.g., biopolymers) utilized in medical devices are obtained from a variety of sources including, for example, starch and cellulose derived from plants, or hyaluronic acid derived from bacterial sources.

a. Possible Naming Convention

The source of the material (e.g., type, species) could be important to identify in the name of naturally-derived materials in a materials listing.

b. Other Labeling Considerations

The predominant type or types of naturally-derived material could be identified in a materials listing for naturally-derived materials. Naturally-derived materials often contain other types of molecules that co-purify during processing; however, it may be reasonable to only include the constituent intended to be in the material in the listing, unless the constituent poses toxicity risks. Purity is important for these products, and it could be helpful to include in the labeling the chemical names of the processing reagents such as cross-linkers, and safe limits for chemicals that pose toxicity risks such as heavy metals and endotoxins. It may be appropriate for some devices to include additional information in a naturally-derived materials listing, as described in available device-specific guidance,[24] FDA recognized consensus standards, or based on risks identified during performance testing, similar to the scenario described in the polymer section above.

(6) Composites

Composites are comprised of two or more independent materials that maintain separate distinct material phases. When composites are used, each material has a potential for exposure; therefore, it may be appropriate to independently identify each material as suggested in the respective categories identified in this section (e.g., metals, polymers, etc.). Additional materials created due to an interaction at the interface of the composite materials also may be helpful to disclose, when present.

a. Possible Naming Convention

Similar to polymers, it may be most informative to include a commercial name for the composite if available. In addition, the naming convention of the constituent materials could follow the respective naming convention(s) listed above, as applicable.

(7) Manufacturing Residuals

Devices are often processed in the presence of other manufacturing materials and processing aids that could lead to contamination of the device materials with bulk and/or surface residuals at toxicologically

[24] As an example, please see device-specific guidance document "Guidance Document for Dura Substitute Devices; Guidance for Industry," issued November 9, 2000.

significant levels.[25, 26, 27] If the presence of these residuals in or on the final finished device is not mitigated by subsequent cleaning/processing, it may be informative to list such residuals separately using the relevant naming conventions and labeling considerations discussed above. Sterilization and reprocessing residues are two examples of such residuals.

IV. Conclusions

CDRH recognizes that we are in an era of device and materials innovation, which has led to technological breakthroughs which have greatly improved patients' lives. We also recognize the great level of scope and complexity of materials utilized in medical devices, which can be challenging to communicate in a clear and consistent manner. Input from stakeholders will be critical to further the conversation on how and when materials information is critical for medical devices, and best approaches to ensure communication of this information is provided in a clear and effective manner so that patients and healthcare providers are empowered to make well informed decisions about the use of medical devices.

V. Specific Questions for Stakeholders:

In this discussion paper, CDRH has provided an initial framework to stimulate discussion and to solicit feedback from stakeholders on how materials information could be communicated. CDRH is interested in obtaining public comment and feedback on the following series of questions related to the inclusion of specific materials information in medical device labeling that may be helpful for patients and healthcare providers to make informed decisions regarding medical device use. Please submit your comments regarding this discussion paper to https://www.regulations.gov, Docket No. FDA-2021-N-0334 within 60 days. FDA will consider all comments submitted to this docket (FDA-2021-N-0334) before issuing subsequent documents or draft guidance related to this topic.

General Framework:

1. **What factors might be considered in the development of a framework for medical device labeling where specific materials information could be considered important and relevant for informed decision-making by the patient or healthcare provider?**
2. **Given the wide range of devices in use, for which types of devices could detailed materials information in labeling be appropriate and relevant for informed decision-making by the patient or healthcare provider?**

[25] See, e.g., the FDA website on Ethylene Oxide Sterilization for Medical Devices, https://www.fda.gov/medical-devices/general-hospital-devices-and-supplies/ethylene-oxide-sterilization-medical-devices.

[26] See, e.g., K. Kanemitsu, H. Kunishima, T. Saga, H. Harigae, T. Imasaka, Y. Hirayama, M. Kaku, Residual formaldehyde on plastic materials and medical equipment following low-temperature steam and formaldehyde sterilization, Journal of Hospital Infection, Volume 59, Issue 4, 2005, Pages 361-364, https://www.sciencedirect.com/science/article/pii/S019567010400475X.

[27] See, e.g., Peter L. Goering, W. Don Galloway, Toxicology of Medical Device Materials: Introduction to the symposium presented at the 1988 Annual Meeting of the Society of Toxicology, Fundamental and Applied Toxicology, Volume 13, Issue 2, 1989, Pages 193-195, https://www.sciencedirect.com/science/article/pii/0272059089902558.

Healthcare Provider and Patient Labeling Considerations

3. **What information, if any, could be useful in healthcare provider labeling regarding materials information and/or patient counseling with respect to device materials, and are there any specific concerns related to how materials information may be conveyed in healthcare provider labeling (e.g., language, formatting)?**
4. **What information, if any, could be useful in patient labeling regarding materials information, and are there any specific concerns related to how materials information may be conveyed in patient labeling (e.g., language, formatting)?**

Materials Listings

For each of the material types noted in Section III (1)-(7), please consider the following questions:

5. **Given the variety of different material types, and considering the examples provided in Appendices A and B, how might materials information (e.g., material type, naming convention) be presented in the most clear and consistent manner to healthcare providers and patients?**
6. **What information is most important to provide to communicate potential risks of different types of materials, for example:**
    - **For metals, the minimum specification for constituent elements**
    - **For polymers, the listing of known toxicants, compositions**
    - **For ceramics, the listing of stabilizers**
    - **For natural materials, the purity, presence of toxicants, or processing reagents**
    - **For composites, how constituent material types are listed and/or prioritized**
    - **For manufacturing residuals, the residual thresholds evaluated/tested and/or if the device is processed in a facility with chemicals of known high toxicity**
7. **If there are any medical device materials that you use/are concerned about that do not fit into the material types noted in Section III (1)-(7) of the discussion paper, what are they, and how might they be addressed in medical device labeling?**

Please submit your responses to these questions to https://www.regulations.gov, Docket No. FDA-2021-N-0334 within 60 days.

Appendix A: Example labeling

The following are hypothetical examples of materials listings for each material category: the current general labeling (column 1), and a possible specific labeling (column 2). Each example is presented with basic material information and an alternative scenario that is intended to facilitate public discussion regarding the disclosure of additional specificity in materials in labeling for medical devices, intended for either the healthcare provider or patient.

CDRH has proposed example labeling approaches for material categories listed below:

Metals:

Current General Labeling	Possible Specific Labeling
Made from CoCr alloy	CoCr alloy (ASTM F1537 Alloy 3), which contains*: Cobalt Chromium Molybdenum Aluminum Lanthanum

*Other materials may be present at trace levels.

Polymers:

Current General Labeling	Possible Specific Labeling
Made from acrylic	[Polymer Trade Name]™, Acrylate which contains*: polymethyl methacrylate

*Other materials may be present at trace levels.

Current General Labeling	Possible Specific Labeling
Made from UHMWPE	[Polymer Trade Name]™ Ultra-high Molecular Weight Polyethylene (UHMWPE), which contains*: Polyethylene Vitamin E (amt in ug)

*Other materials may be present at trace levels.

Ceramics:

Current General Labeling	Possible Specific Labeling
Made from zirconia	Contains the following ceramics*: Zirconium oxide Yttrium oxide

*Other materials may be present at trace levels.

Naturally-Derived Materials (Animal Source):

Current General Labeling	Possible Specific Labeling
Made from collagen	Contains the following naturally occurring material*: Type I collagen derived from pig skin Fixative: glutaraldehyde

*Other materials may be present at trace levels

Naturally-Derived Materials (non-Animal Source):

Current General Labeling	Possible Specific Labeling
Made from hyaluronic acid	Contains the following: naturally occurring material*: Hyaluronic acid (bacterial fermentation origin) with Molecular weight range of Phosphate Buffered Saline 1,4-butanediol diglycidyl ether (BDDE) Residual Proteins Bacterial Endotoxin

*Other materials may be present at trace levels

Composite:

Current General Labeling	Possible Specific Labeling
Made from carbon fiber reinforced PEEK	Contains the following composite materials*: [Polymer Trade Name] PEEK which contains: Polyether-ether-ketone [Polymer Trade Name] Carbon Fiber which contains: Carbon fiber

*Other materials may be present at trace levels

Appendix B: Device Examples

The following are hypothetical examples of materials listings for devices made of multiple materials or which have multiple constituents. Each example is presented to demonstrate how labeling for medical devices, intended for either the healthcare provider or patient, could potentially be structured to disclose multiple materials in a transparent way for devices with different levels of contact.

Orthopedic device labeling example for a total hip replacement implant

DEVICE MATERIALS	
Device component(s)	**Material content**
FDAMax® Acetabular shell	Titanium alloy (ASTM F136) which contains*: Titanium Aluminum Vanadium Iron
FDAProx® Acetabular shell porous bead coating	Titanium alloy (ASTM F67) which contains*: Titanium Iron
FDAProx® Acetabular liner	[Polymer Trade Name 1]™ Ultra-high molecular weight polyethylene which contains*: Polyethylene Tocopherol (Vitamin E)
FDAFemoHe® Femoral head	Cobalt-Chromium-Molybdenum alloy (ASTM F1537) which contains*: Cobalt Chromium Molybdenum Aluminum Nickel Silicon Iron Manganese Lanthanum
FDAStem® Femoral stem	Titanium alloy (ASTM F136) which contains*: Titanium Aluminum Vanadium Iron
FDAStem® Femoral stem coating	Contains the following ceramic*: Hydroxy-apatite

*	Other materials may be present at trace levels

Cardiovascular device labeling for a heart valve

DEVICE MATERIALS	
Device component	**Material content**
FDAFlexpro® Stent frame	Nitinol (ASTM F2063) which contains*: Nickel Titanium Iron Chromium Copper Niobium
FDAFlexpro ® Radiomarker	Tantalum*
FDAFlexpro ® skirt material	[Polymer Trade Name 1]™ Expanded PTFE which contains*: polytetrafluorethylene
FDAFlexpro ® valve material	Contains the following naturally occurring material*: Processed bovine pericardium tissue Fixative: glutaraldehyde
FDAFlexpro® suture	[Polymer Trade Name 2]™ which contains*: Polypropylene
*	Other materials may be present at trace levels

Example device labeling for a repeat use device (insulin pump)

DEVICE MATERIALS	
Device component	**Material content**
FDAPump® Cannula	[Polymer Trade Name 1]™ which contains*: Fluorinated Ethylene Propylene (FEP)
FDAPump® Reservoir	[Polymer Trade Name 2]™ which contains*: Polypropylene

FDAPump® Housing	[Polymer Trade Name 3]™ which contains*: Polycarbonate
FDAPump® Adhesive Pad	[Polymer Trade Name 4]™ Acrylic Adhesive which contains*: Ethylacrylate n-Butylacrylate
	Non-woven Polyester Backing
FDAPump® Fill Syringe	Barrel: [Polymer Trade Name 2]™ which contains*: Polypropylene
	Plunger: [Polymer Trade Name 4]™ which contains*: Polyethylene
FDAPump® Fill Needle	Stainless steel (ASTM F899) which contains: Iron Chromium Nickel Manganese Silicon
FDAPump® Remote Controller	Housing: [Polymer Trade Name 5]™ which contains*: Polycarbonate
	Test Strip Port: polyphthalamide (PPA)
*	Other materials may be present at trace levels

Example device labeling for an indwelling catheter

DEVICE MATERIALS	
Device component	**Material content**
FDAPICC® Catheter Body, Tip,	[Polymer Trade Name 1]™ which contains*: Polyether-polyurethane Color: Phthalocyanine Blue (CAS 147-14-8)

FDAPICC® Catheter Lumen Plug, Hubs	[Polymer Trade Name 2]™ which contains*: Polyether-polyurethane Color: Phthalocyanine Green (CI 74260)
FDAPICC® Catheter Extension Lines	[Polymer Trade Name 3]™ which contains*: Polyether-polyurethane
FDAPICC® Extension Line Clamps	[Polymer Trade Name 4]™, which contains*: Acrylic-polycarbonate
*	Other materials may be present at trace levels

Example device labeling for a Bone Cement

DEVICE MATERIALS	
Device component	**Material content**
FDACment®	Poly (methyl methacrylate)
FDACment® Powder	[Trade Name 1] which contains*: Methylmethacrylate-styrene-copolymer Benzoyl peroxide (BPO, initiator)
FDACment® Liquid	[Trade Name 2] which contains*: Methyl methacrylate (MMA, monomer) N,N-Dimethyl-p-toluidine (DMPT, accelerator) Hydroquinone (stabilizer)
*	Other materials may be present at trace levels

Example device labeling for a Bone Grafting Material

DEVICE MATERIALS

Device component	Material content
FDABoneBlock® Collagen	Type I collagen derived from porcine epidermis (pig skin)
FDABoneBlock® HA	Hydroxyapatite *: Sourced from bovine femur *:
*	Other materials may be present at trace levels