**Biocompatibility**

*【Studies supporting biocompatibility and assessing toxicology are to be in cluded in this section. Studies to assess the immunological response to animal or human tissues, tissue components or derivatives are to be included in this section. This should include:*

*A list of all materials in direct or indirect contact with the tissue or user.*

*State conducted tests, applied standards, test protocols, the analysis of data and the summary of results*

*A discussion of the non-clinical testing considered for the device and support for their selection or omission from the verification and validation studies conducted in this category (i.e. what tests were considered and why they were or were not performed)*

*Discussion to support why the evidence presented is sufficient to support the application.】*

**1 Tissue Contacting Products/Components/Materials**

***【****Please consult the Biocompatibility Guidance Document for considerations regarding the biocompatibility of your device.*

*Resources*

*Guidance:“Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"”****】***

* 1. **How many tissue contacting products/components/materials are there?**

*【Tissue contacting includes blood contacting, per the Agency’s guidance document “Use of International Standard ISO 10993-1, “Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process” ”Guidance Document. Tissue contacting includes any direct or indirect contacting product, components, or materials.*

*Separate testing may be needed (i.e., increase the number of products/components/materials there are in the dropdown), if components of the device have different nature or duration of tissue contact, or any device components are made of novel material(s).*

*If multiple materials or components share the same contact type, duration of contact, and justification for why no testing is needed, they together may be considered a single product or component when choosing the number of tissue contacting products/components/materials.*

*For example:*

*If you have multiple tissue contacting products/components/materials that all share the same nature of body contact, contact duration, and justification for why no testing is being provided, choose “1”.*

*If you have two groups products/components/materials, and within each group they have the same contact type, duration of contact, and justification for why no testing is being provided, choose “2”.*

*Resources*

*Guidance:“Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"”****】***

**1.2 Tissue Contacting Material 1**

1.2.1 Identify the device(s) / accessory(ies) / component(s) that directly or indirectly contacts the tissue.

1.2.2 Please state the exact name and any identifiable information for the particular material used.

1.2.3 If color additives are included, please identify them here. If no color additives are included, state "N/A."

*【For 510(k): Please identify the tissue contacting color additives.*

*For De Novo: Please state “N/A” in the textbox.*

*For PMA: Please identify the following:*

1. *The color additive common and chemical name,*
2. *The amount of each color additive in the formulation by weight percent of the colored component, and*
3. *The total amount (e.g., ug, ppm) of color additive in the device.*

*Resources*

*Color Additives Website*

*<https://www.fda.gov/industry/color-additives>*

*】*

1.2.4 Choose intended contact of the particular material.

*【Direct contact - term used for a device or device component that comes into physical contact with body tissue.*

*Indirect contact - term used for a device or device component through which a fluid or gas passes, prior to the fluid or gas coming into physical contact with body tissue (in this case the device or device component itself does not physically contact body tissue).*

*For more information refer to Guidance Document “Use of International Standard ISO 10993-1, “Biological evaluation of medical devices - Part 1: Evaluation and testing with a risk management process.””】*

1.2.5 Is there a potential for repeat exposure?

*【Repeat exposure could be during a procedure or during multiple procedures/device uses. During a procedure, a patient might have multiple devices used or implanted, so the dose of a tissue contacting material would be higher than with use of a single device. Multiple uses also could be outside a single procedure, such as for dialysis where a patient might have 2-3 dialysis procedures each weak.】*

1.2.6 Choose the type of tissue contact of your tissue contacting material.

1.2.7 Duration of Contact

*【Transient contact - term used for a device or device component that comes into very brief/transient contact with body tissue (e.g., hypodermic needles that are used for less than one minute).*

*For devices with transient contact, assessment of biocompatibility risk should be conducted to determine if testing is needed (for more information refer to Guidance Document “Use of International Standard ISO 10993-1,‘Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process’”).】*

1.2.7.1 Cytotoxicity(Cytotoxicity Testing)

1.2.7.1.1 What type of cytotoxicity testing was conducted?

Direct Contact Method

Extraction Method (MEM Elution)

Another method (explained below)

None (justified below)

ASCA (MEM)

*【The following content is based on ISO 10993-5 and ASTM F813-07.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.2 Sensitization(Sensitization Testing)

1.2.7.2.1 What type of sensitization testing was conducted?

Guinea Pig Maximization Test (GPMT)

LLNA (per ASTM F 2148)

Buehler Dermal Sensitization (per ISO 10993-10)

Another method

None (justified below)

ASCA (GPMT)

ASCA (Buehler)

*【The following content is based on ISO 10993-10.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.3 Irritation(Irritation Testing)

1.2.7.3.1 What type of irritation testing was conducted?

Intracutaneous Irritation Test

Dermal Irritation Test

Ocular Irritation Test

Mucosal Irritation Test

Another method (explained below)

None (justified below)

ASCA (Intracutaneous)

ASCA (Dermal, Extract)

*【The following content is based on ISO 10993-10.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.4 Acute Systemic & Pyrogenicity

1.2.7.4.1 Acute Systemic Toxicity Testing

*【The following content is based on ISO 10993-11.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.4.2 Material Mediated Pyrogenicity Testing

*【The following content is based on ISO 10993-11 and USP<151>.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.5 Subacute/Subchronic(Subacute/Subchronic Toxicity Testing)

Specific questions for this test do not exist yet in this template or the FDA reviewer's Smart Templates. We recommend Subacute/Subchronic Toxicity be assessed. If testing is performed, we recommend it be conducted per ISO 10993-11. You may also like to consult the FDA supplemental information sheet for this testing. Please provide a test report in an attachment in the Biocompatibility Reports and Documentation section below, or provide a justification for why testing was not conducted in the Comments below.

1.2.7.6 Genotoxicity(Genotoxicity Testing)

Specific questions for this test do not exist yet in this template or the FDA reviewer's Smart Templates. We recommend Genotoxicity Toxicity be assessed. If testing is performed, we recommend it be conducted per ISO 10993-3 and ISO/TR 10993-33. You may also like to consult the FDA supplemental information sheet for this testing. Please provide a test report in an attachment in the Biocompatibility Reports and Documentation section below, or provide a justification for why testing was not conducted in the Comments below.

1.2.7.7 Implantation(Implantation Testing)

Specific questions for this test do not exist yet in this template or the FDA reviewer's Smart Templates. We recommend Implantation Toxicity be assessed. If testing is performed, we recommend it be conducted per ISO 10993-6. You may also like to consult ASTM F981-04, F1408-97, F1983-99, and F763-05 for more information, as well as the FDA supplemental information sheet for this testing. Please provide a test report in an attachment in the Biocompatibility Reports and Documentation section below, or provide a justification for why testing was not conducted in the Comments below.

1.2.7.8 Hemocompatibility (Hemocompatibility Testing)

1.2.7.8.1 Hemolysis Testing

Yes, Direct and Indirect Contact testing

Yes, Direct contact only

Yes, Indirect contact only

No

ASCA

*【The following content is based on ASTM F756 and ISO 10993-4.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.8.2 Complement Activation Testing

Yes, SC5b-9

No

ASCA

*【The following content is based on ASTM F 1984, ISO 10993-4, and ISO 10993-20.*

*Under the ASCA (Accreditation Scheme for Conformity Assessment) Pilot, the FDA grants ASCA Recognition to qualified accreditation bodies to accredit testing laboratories to perform premarket testing for medical device companies. If you used an ASCA-accredited testing laboratory to conduct this testing, and an ASCA summary test report was provided, please indicate this.】*

1.2.7.8.3 Thrombogenicity Testing

1.2.7.8.4 Specific questions for this endpoint do not exist yet in this template or the FDA reviewer's Smart Templates. We recommend Hemocompatibility be assessed to include evaluation of hemolysis, complement activation and thrombogenicity. If testing is conducted to address these endpoints, we recommend the following be considered.

HEMOLYSIS: For hemolysis testing of devices having direct contact with circulating blood, we recommend that both direct and indirect (extract) hemolysis testing be conducted. For hemolysis testing of devices having indirect contact with circulating blood, we recommend that only an indirect (extract) method be conducted. Please also see the Biocompatibility Guidance and ASTM F756, and ISO 10993-4.

COMPLEMENT ACTIVATION: For complement testing of devices having direct contact with circulating blood, we recommend that SC5b-9 testing be conducted. We recommended that you include the predicate as an additional control in the SC5b-9 complement activation testing, if the predicate device 510k application investigated only C3a complement activation testing, or if there is a statistically significant difference between your device and the negative control. Please also see the Biocompatibility Guidance and ASTM F1984, ISO 10993-4, and ISO 10993-20.

THROMBOGENICITY: For devices having direct contact with circulating blood, we recommend that thrombogenicity be evaluated. If anticoagulated in vivo models or in vitro models are used, please contact FDA to discuss your proposed methods prior to initiation of the studies to ensure that the studies will be adequately designed to address FDA's concerns. Use of the Q-submission process may be helpful. Please provide a test report in an attachment in the Biocompatibility Reports and Documentation section below, or provide a justification for why testing was not conducted in the Comments below. Please also see the Biocompatibility Guidance and ISO 10993-4.

1.2.7.9 Chronic(Chronic Toxicity Testing)

Specific questions for this test do not exist yet in this template or the FDA reviewer's Smart Templates. We recommend Chronic Toxicity be assessed. If testing is performed, we recommend it be conducted per ISO 10993-11. You may also like to consult the FDA supplemental information sheet for this testing. Please provide a test report in an attachment in the Biocompatibility Reports and Documentation section below, or provide a justification for why testing was not conducted in the Comments below.

1.2.7.10 Carcinogenicity

Specific questions for this endpoint do not exist yet in this template or the FDA reviewer's Smart Templates. We recommend Carcinogenicity be assessed. If in rare cases testing is needed, please contact FDA to discuss your proposed methods prior to initiation of the studies to ensure that the studies will be adequately designed to address FDA's concerns. Use of the Q-submission process may be helpful. Please provide the carcinogenicity assessment, or if applicable, the carcinogenicity test report in an attachment in the Biocompatibility Reports and Documentation section below. Please also see the Biocompatibility Guidance.

**2 Biocompatibility Reports and Documentation**

Please attach any documentation (e.g., test reports) pertaining to the biocompatibility of your device. If no test reports were attached, please attach a rationale explaining why testing is not necessary.