Contains Nonbinding Recommendations

Biocompatibility Testing of Medical Devices – Standards Specific Information for the Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program

---

Guidance for Industry, Accreditation Bodies, Testing Laboratories, and Food and Drug Administration Staff

Document issued on September 25, 2020.
The draft of this document was issued on September 23, 2019.

For questions about this document regarding CDRH-regulated devices, contact the ASCA Pilot Program at ASCA@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov.

The OMB control number for this information collection is 0910-0889 (expires 06-30-2023).

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2019-D-3805. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

CDRH

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 20012 and complete title of the guidance in the request.

CBER

Additional copies are available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach, and Development (OCOD), 10903 New Hampshire Ave., WO71, Room 3128, Silver Spring, MD 20903, or by calling 1-800-835-4709 or 240-402-8010, by email, ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

Table of Contents

Biocompatibility Testing of Medical Devices – Standards Specific Information for the Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program

Guidance for Industry, Accreditation Bodies, Testing Laboratories, and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

This guidance provides information on how the Biological Evaluation of Medical Devices standards are incorporated into the Pilot Accreditation Scheme for Conformity Assessment Program (hereafter referred to as the ASCA Pilot). The ASCA Pilot is described in FDA's guidance The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program.[1]

For the edition of the FDA-recognized consensus standard(s) included in the ASCA Pilot, see the FDA Recognized Consensus Standards Database.[2] For more information regarding use of consensus standards in regulatory submissions, please refer to the FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices[3] and Standards Development and the Use of Standards in Regulatory Submissions Reviewed in the Center for Biologics Evaluation and Research.[4]

[1] Available at: The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program
[2] Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
[3] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices
[4] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/standards-development-and-use-standards-regulatory-submissions-reviewed-center-biologics-evaluation

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidance means that something is suggested or recommended, but not required.

II. Scope

This guidance includes the following:

- A list of the FDA-recognized consensus standards and test methods included in the ASCA Pilot for biocompatibility testing of medical devices;
- The program specifications for the FDA-recognized consensus standards and test methods in the ASCA Pilot for biocompatibility testing of medical devices; and
- The recommended premarket submission contents specific to FDA-recognized consensus standards and test methods for biocompatibility testing of medical devices when testing is conducted by an ASCA-accredited testing laboratory.

FDA's guidance The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program describes how accreditation bodies, testing laboratories, device manufacturers, and FDA staff participate in the ASCA Pilot as well as how FDA-recognized consensus standards and test methods are selected and how program specifications are developed.

Please see FDA's guidance Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"[5] for recommendations on biocompatibility testing to support a premarket submission. The ASCA Pilot for biocompatibility testing of medical devices does not include certain types of devices that require customized sample preparation and/or testing methodologies, or absorbable and *in situ* polymerizing devices, liquid devices, creams, gels, hydrogel devices, and devices containing nanomaterials.

III. List of FDA-Recognized Consensus Standards and Test Methods in the ASCA Pilot for Biocompatibility Testing of Medical Devices

Biological evaluation assesses the biocompatibility-related risks of medical devices with direct and/or indirect contact with human tissue. When biocompatibility testing is needed as part of a premarket submission to FDA to address biocompatibility-related risks, the selected, cross-cutting biological evaluation standards listed below are relevant to many manufacturers and the device types are of significant public health importance.

[5] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and

- ASTM F756: *Standard Practice for Assessment of Hemolytic Properties of Materials*
- ASTM F720: *Standard Practice for Testing Guinea Pigs for Contact Allergens: Guinea Pig Maximization Test*
- ISO 10993-4: *Biological evaluation of medical devices – Part 4: Selection of tests for interactions with blood*
- ISO 10993-5: *Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity*
- ISO 10993-10: *Biological evaluation of medical devices – Part 10: Tests for irritation and skin sensitization*
- ISO 10993-11: *Biological evaluation of medical devices – Part 11: Tests for systemic toxicity*
- USP <151>: *Pyrogen Test*
- ISO 10993-12: *Biological evaluation of medical devices – Part 12: Sample preparation and reference materials*

The eligible test methods included in the ASCA Pilot for biocompatibility testing of medical devices are:

FDA-Recognized Consensus Standard	Test method(s)
ISO 10993-4*	Complement Activation using a U.S. marketed ELISA kit
ISO 10993-4 and ASTM F756	Direct and Indirect Hemolysis
ISO 10993-5	MEM Elution Cytotoxicity
ISO 10993-10[6]	Dermal Irritation, Intracutaneous Reactivity Irritation, and Closed Patch Sensitization
ISO 10993-10 and ASTM F720[7]	Guinea Pig Maximization Sensitization
ISO 10993-11	Acute Systemic Toxicity
ISO 10993-11 and USP 151	Material-Mediated Pyrogenicity
ISO 10993-12	Sample preparation for all test types

* See also ISO/TS 10993-20 for information on when complement activation should be considered for anaphylaxis (Table 2, Hypersensitivity Column).

The extent of FDA recognition (complete or partial) is provided in the Supplemental Information Sheet (SIS) for each standard listed in the FDA Recognized Consensus Standards Database.[8] The SIS provides additional information to consider when using FDA-recognized consensus standards, such as relevant guidance documents that provide clarity on FDA recommendations for testing to support premarket submissions.

[6] We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method. See generally: https://www.fda.gov/science-research/advancing-regulatory-science/vi-modernizing-safety-testing

[7] *Ibid*

[8] Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

IV. Accreditation and Assessment of Testing Laboratories by ASCA-Recognized Accreditation Bodies

A. Scope of Assessments

Section 7 of ISO/IEC 17011: *Conformity assessment – Requirements for accreditation bodies accrediting conformity assessment bodies* (hereafter referred to as "ISO/IEC 17011") describes processes by which accreditation bodies assess testing laboratories. In order to maintain conformance to ISO/IEC 17011, an accreditation body assesses a sample of the scope of accreditation of its accredited testing laboratories at least every two years.[9] When assessing a testing laboratory under the ASCA Pilot, an accreditation body is expected to assess all (and not a sample of) biological evaluation standards and test methods. That is, in the ASCA Pilot, ASCA-recognized accreditation bodies are expected to assess all (and not a sample) of the biological evaluation of medical devices standards and test methods in order to ensure competence across the testing laboratory's scope of *ASCA Accreditation*.

B. ASCA Program Specifications for Biocompatibility Testing of Medical Devices

The ASCA program specifications in this section provide expectations for the accreditation of testing laboratories for the biocompatibility testing of medical devices under the ASCA Pilot. ASCA-recognized accreditation bodies, following the processes of ISO/IEC 17011, accredit testing laboratories to all relevant elements of ISO/IEC 17025: 2017: *General requirements for the competence of testing and calibration laboratories* (hereafter referred to as "ISO/IEC 17025") as well as the ASCA program specifications identified in this section. In addition, all testing should be conducted considering the recommendations in the CDRH Biocompatibility policy as described in FDA's guidance Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process." For readability and ease of reference, the numbering and nomenclature (including the term "requirements")[10] below correspond to the numbering and nomenclature of clauses/subclauses in ISO/IEC 17025.

ISO/IEC 17025 Section 4 "General requirements"

4.1 Impartiality

If any services, such as consulting, design, or research, are offered by the testing laboratory, it agrees to have a policy and procedure for maintaining impartiality through separation of those services from its testing activities.

A device manufacturer's internal testing laboratory agrees to have policies and procedures that specifically ensure and protect the impartiality of the laboratory to test or otherwise

[9] *See* 7.9.3 of ISO/IEC 17011: 2017: *Conformity assessment – Requirements for accreditation bodies accrediting conformity assessment bodies*.

[10] Some definitions within voluntary consensus standards refer to "requirements." FDA's references to them for the ASCA Pilot do not make them legal or regulatory requirements unless specifically identified as such.

evaluate devices manufactured by the laboratory's parent organization and, if applicable, other manufacturers without regard to the impact of the test results on the parent organization's business interests.

4.2 Confidentiality
There are no additional specifications above those set forth in ISO/IEC 17025.

ISO/IEC 17025 Section 5 "Structural requirements"
There are no additional specifications above those set forth in ISO/IEC 17025.

ISO/IEC 17025 Section 6 "Resource requirements"

6.1 General
There are no additional specifications above those set forth in ISO/IEC 17025.

6.2 Personnel

a) The testing laboratory agrees to maintain competent technical personnel that are knowledgeable in appropriate test method for the requested scope of accreditation:
    - For technicians performing in vivo tests, 1 year of relevant test experience with each standard test included in the ASCA program to which technicians are assigned OR demonstrated proficiency through completion minimally of 25 tests OR 25 phases as outlined in each study specific training and:
        - Bachelor's or associate degree in relevant science areas to the in vitro/in vivo biocompatibility testing included in the ASCA Pilot, OR
        - a high school degree, and at least one of the following laboratory technician accreditations: Laboratory Animal Technician (LAT), Assistant Laboratory Animal Technician (ALAT), and/or Laboratory Animal Technologist (LATG).
    - For technicians performing in vitro tests 1 year of relevant test experience with each standard test included in the ASCA program to which technicians are assigned, OR demonstrated proficiency through completion minimally of 25 tests, OR 25 phases as outlined in each study specific training and:
        - Bachelor's or associate degree in relevant science areas to the in vitro/in vivo biocompatibility testing included in the ASCA Pilot.
    - For technicians performing any test specific (e.g., for complement activation) sample preparation, 1 year of sample preparation experience with the relevant standard test included in the ASCA program to which technicians are assigned, OR demonstrated proficiency through completion of sample preparation for minimally 25 tests as outlined in each study specific training and:
        - Bachelor's or associate degree in science.
    - For technicians performing sample preparation that is applicable for various tests (e.g., technicians in general sample preparation lab who prepare samples/extracts for various tests), 1 year sample preparation experience with any standard test included in the ASCA program OR demonstrated

proficiency through completion of sample preparation for minimally 25 of any of the standard tests in the ASCA program and:
  - Bachelor's or associate degree in science.
- For study directors:
  - Bachelor's or higher degree in scientific discipline; AND
  - 2 years of relevant test experience with each standard test; AND
  - Direction of at least 25 studies in each relevant test, OR management of 25 studies with someone who has directed at least 25 studies in each relevant test.

b) The testing laboratory's management agrees to be knowledgeable in applicable aspects of the FD&C Act and 21 CFR regulations pertinent to the oversight of medical devices and the criteria set out in ISO/IEC 17025 and ASCA program specifications. The testing laboratory further agrees to maintain a list of laboratory managers and contact information.

c) The testing laboratory agrees to:
   - Document and maintain a training program for new and previously trained technical personnel, which will include the proper procedures for applying new/updated test procedures and performing required tests.
   - Provide new and previously trained technical personnel relevant test-specific requalification training (e.g., cytotoxicity subjective scoring) every 6-12 months, or when test standards or procedures are updated or developed, as well as when responsibilities have changed.
   - Conduct training on a periodic basis through application of training approaches, such as on-the-job training and formal classroom training, as appropriate.
   - Document and maintain records of training demonstrating that technical personnel who participate in the conduct of ASCA testing have been trained and evaluated to be competent in the performance of each ASCA test. The training includes the ability to follow test-related standard operating procedures (SOPs) and documentation, and in person hands-on training. Training may also include classroom (or online) training. Testing laboratories further agree to have predefined criteria to qualify that technical personnel (technicians and study directors) can perform assigned tasks related to the tests under the scope of *ASCA Accreditation,* and for when retraining will be needed.
   - Establish procedures for periodic internal test lab proficiency checks of technicians (e.g., blind scoring of negative and positive controls for MEM elution assays) for the tests performed under the ASCA Pilot with subjective analyses, to include when staff would require retraining (e.g., protocol non-conformance, change in assigned activities).
   - Maintain records demonstrating trainers have qualifications and at least 2 years' experience (routinely performing each relevant ASCA test) to train the technical personnel who will perform the ASCA tests.

d) The testing laboratory agrees to have procedures to establish how test and control samples are prepared and training that includes at a minimum the following:
    - Procedures for device preparation, including:
        - Cutting samples (if appropriate) and documentation (e.g., photographs) of any particle generation prior to extraction,
        - Determination of device surface area for extraction ratio, and the volume required to complete the study,
        - Use of non-standard surface area approaches (e.g., porous devices),
        - Exclusion of non-contacting components from extraction,
        - Selection of representative portions for direct contact hemocompatibility studies (i.e., hemolysis, complement activation),
    - Selection of extraction conditions (i.e., time, temperature, and extraction vehicle),
    - Assessment and documentation of changes (e.g., photographs) after extraction to sample (e.g., color changes, integrity, swelling) or extract conditions (e.g., pH, particles/precipitates, color changes, or turbidity),
    - General and/or test-specific follow-up procedures when changes are noted (e.g., extract settling techniques to allow particle-free IV injections),
    - Use of non-standard extraction approaches (e.g., fluid path approaches, approaches for extremely large devices, procedures to maintain contact with extraction vehicle), and
    - Handling of extracts prior to testing (e.g., filtration, centrifugation, storage time and temperature).

e) In addition, for *in vitro* testing, the testing laboratory agrees that training will include the following, at a minimum:
    - MEM elution cytotoxicity:
        - Cell line maintenance
        - Cell counting
        - Cell seeding
        - Addition of test and control samples to the cell cultures
        - Scoring of test and control articles
        - Mock study to assess technician competence in test performance, data documentation, and result interpretation (including test-specific assessment of borderline results)
        - Minimally, biannual periodic technician proficiency check of negative and positive control scoring, and additional technician retraining, if needed
    - Hemolysis:
        - Timing from blood collection to use in test
        - Hemoglobin absorbance standard curve
        - Dilution procedures and dilution factor calculations
        - Sample and control preparation and documentation
        - Representative sample selection(may apply to both direct and indirect contact tests)

  - Documentation of supernatant color and presence of dispersed pellet fragments, if any
  - Documentation of presence or absence of pellet, pellet size, and color after centrifugation if different than negative control
  - Supernatant removal to preserve pellet
  - Blank sample correction (including if an extract is colored)
  - Hemolytic index calculation
  - Mock study to assess technician competence in test performance, data documentation, and result interpretation
  - Technician retraining, if needed
- Complement activation:
  - Serum/blood/plasma handling to minimize complement activation
  - Sample and control preparation and documentation
  - Representative sample selection
  - Small volume pipetting
  - Complement absorbance standard curve
  - Dilution procedures and dilution factor calculations
  - Exposure time
  - Complement concentration calculations
  - Test validation criteria
  - Data analysis and use of historical control data, if necessary
  - Mock study to assess technician competence in test performance, and data documentation, and result interpretation
  - Technician retraining, if needed

f) For *in vivo* studies, as part of the general animal handling training, the testing laboratory agrees that training will include the following, at a minimum:
   - Test-specific animal selection criteria
   - Animal identification and traceability within and across studies (e.g., for pyrogenicity)
   - Species- and test-specific animal holding techniques
   - Test-specific acclimation techniques
   - Body weight measurement
   - Species-specific in life observations (e.g., cage accidents, decline in health, seizures, weight loss, breathing difficulties) and when veterinarian oversight should be requested
   - Test-specific data documentation, calculations, and result interpretation (including test-specific assessment of borderline results, and re-challenge or re-test criteria, when applicable)
   - Technician retraining, if needed

g) For the following specific *in vivo* tests, the application organization agrees that training will include the following, at a minimum:
   - Guinea Pig Maximization (GPMT) and Closed Patch Sensitization:
     - Shaving techniques (e.g., to avoid razor burn)

  - Mixing of extract and adjuvant, if applicable
  - Intradermal injection (GPMT) including criteria to confirm avoidance of subcutaneous injections
  - Sample application (GPMT and Closed Patch)
  - Animal wrapping
  - Differentiation for source of redness (e.g., true sensitization versus mechanical/adhesive irritation)
  - Minimally, quarterly periodic technician proficiency check of positive control scoring (in live animals at least once annually)
  - Technician retraining, if needed
- Intracutaneous Reactivity and Dermal Irritation:
  - Shaving techniques (e.g., to avoid razor burn)
  - Application of test samples
  - Injection technique and signs to confirm appropriate injection location
  - Differentiation for source of redness (e.g., true irritation versus possible irritation from shaving)
  - Minimally, biannual periodic technician proficiency check of positive response scoring (in live animals at least once annually)
  - Technician retraining, if needed
- Acute Systemic Toxicity:
  - Balance use and calibration to ensure appropriate sensitivity
  - Intraperitoneal (IP) and intravenous (IV) injection techniques and signs to confirm appropriate injection location
  - Minimally, technician proficiency check on injection techniques prior to conduct of next test if it has been more than one month between technician conduct of a study
  - Technician retraining, if needed
- Material-mediated pyrogenicity:
  - Use of pyrogen-free/depyrogenated glassware and pyrogen free saline for extraction
  - Temperature probe use and calibration to ensure appropriate sensitivity
  - Intravenous (IV) injection techniques and signs to confirm appropriate injection location
  - Technician retraining if needed.

6.3 Facilities and environmental conditions

Lab personnel should be aware of the FD&C Act and regulations as applicable to medical device manufacturers. Under 21 CFR 820.50, Purchasing Controls, medical device manufacturers must communicate as part of contracted work any environmental conditions necessary for the proper conduct of testing done under the scope of accreditation. In addition, testing laboratories should have policies and procedures in place to implement 21 CFR part 58, Good Laboratory Practices, for Nonclinical Laboratory Studies.

6.4 Equipment

a) The testing laboratory agrees to ensure that all equipment used for testing and evaluating devices is available and in proper working order for the requested scope of accreditation.

b) The testing laboratory agrees to ensure that its procedures address adding, deleting, modifying, or maintaining information in equipment records in an accurate and timely manner, and specify the personnel responsible for these tasks.

c) The testing laboratory agrees to ensure that its procedures specify the steps for establishing calibration intervals for each type or item of equipment, and specify criteria, steps, and approvals for extending the calibration interval of an instrument.

d) The testing laboratory agrees to have procedures to examine the effects of equipment operation outside the equipment tolerances or study specified limits (e.g., temperature excursions) on test results. The procedures identify the personnel responsible for such examination of the equipment (e.g., technicians) and determination of acceptability with respect to test validity (e.g., study directors/toxicologists), specify their responsibilities, and provide the steps for determining if the equipment variation would impact the study results, including:
    - Determining whether the effects are unacceptable (including the accept/reject criteria);
    - Identifying the conducted tests affected;
    - Analyzing the results impacted for these particular tests; and
    - Determining whether retesting is required.

6.5 Metrological traceability

a) Testing laboratories agree to use specified methods and/or standards that clearly describe the following:
    - Calibration to three decimal places for spectrophotometer absorbance readings for hemolysis and complement activation, and
    - Particle ranges for calibration of coulter counter use for cell counting.

b) If test-specified positive, negative, and/or reference controls are no longer able to distinguish between positive and negative responses, the testing laboratory agrees to have procedures to qualify new controls.

c) The testing laboratory agrees that controls (positive/negative/reagent, if applicable) will meet assay-specific acceptance criteria.

d) The testing laboratory agrees that, when concurrent positive controls are not conducted with the test article (i.e., sensitization testing), biannual testing (i.e., within 3 months of the test article) will be conducted to confirm the ability of the test system to detect a positive sensitization response. If it is determined that the periodic positive control is no longer valid, all testing conducted after the last validated positive control run cannot be submitted as part of the ASCA Pilot.

6.6 Externally provided products and services

a) The testing laboratory agrees to ensure that any subcontractors utilized to conduct testing under the scope of *ASCA Accreditation* are ASCA-accredited testing laboratories for the selected tests.

ISO/IEC 17025 Section 7 ("Process requirements")

7.1 Review of requests, tenders and contracts
There are no additional specifications to those set forth in ISO/IEC 17025.

7.2 Selection, verification and validation of methods

a) The testing laboratory agrees that its management system will include procedures governing the development, maintenance, and use of test procedures (including associated documents such as test data forms and checklists). These management system procedures include steps for:
    - Identifying the personnel responsible for developing, reviewing, and maintaining these documents
    - Specifying the frequency of review by technical personnel and management
    - Ensuring consistency with applicable standard(s)
    - Ensuring test modifications are reviewed by personnel who are competent to the applicable standard(s)
- Identifying and documenting the types of modifications to the test procedures that do not need to be reviewed by FDA for confirmation prior to implementation, if included in the test lab application. The testing laboratory further agrees that changes (either at the request of study sponsor or initiated by the test lab) to any procedures regarding the following as well as any unanticipated changes will be confirmed with FDA and its Accreditation Body prior to implementation:
    - Changes to sample for retesting to achieve a "passing" result
    - pH adjustments
    - Sample filtration or other extract manipulation
    - Removal or modification of documentation associated with color, turbidity or particles in the test extract, or swelling/degradation of the test article
    - Frequency of non-concurrent control testing
    - Changes to acceptance criteria outside the validated/qualified laboratory-specific limits (e.g., for complement activation where the standard methods do not specify acceptable limits)
    - Changes to data calculations and presentation, if applicable (e.g., hemolytic index, irritation index, complement activation plots)
    - Changes in the criteria for re-challenge or retesting
    - Changes in the criteria for reportable adverse clinical observations or animal deaths

b) The testing laboratory agrees that test procedures will include or specify, as appropriate, the following:

- Unique identification, including title, document number, revision, and effective date;
- Specific test equipment to use along with their required ratings;
- Warnings/caution statements to alert the operators of potential hazards;
- Normal and any unusual ambient conditions (including tolerances) for tests;
- Test data to be obtained and recorded;
- Objective acceptance criteria for results including the essential performance required to be maintained;
- Testing techniques (i.e. test methods) required to ensure consistent results;
- Instructions on test conduct, including equipment operation, reagent preparation, cell line and animal handling, techniques, preparation of test samples (including instructions for sample traceability during testing, if applicable), conduct of each step of the test, data recording, and scoring assessment procedures;
- Deviations from the SOP, as well as any equipment deviations and discussion of why deviations will not impact the validity of the study results.

c) The testing laboratory agrees to ensure that relevant contextual information from the intended use of the device are reflected in the test procedure to ensure that the types of biological evaluation assessments recommended by FDA are considered based on tissue type and duration of contact with the device. In addition, relevant information from the manufacturers essential performance specifications, including any metrological stability, are also reflected in each test procedure to ensure that the test procedures (e.g., extraction temperature and time) are compatible with the device.

d) The testing laboratory agrees to ensure that each test procedure adequately addresses all the applicable specifications of the standard for the devices being tested.

7.3 Sampling

a) The testing laboratory agrees that the procedure(s) for sample preparation will meet the specifications of ISO 10993-12 and FDA's guidance Use of International Standard ISO 10993-1, "Biological evaluation of medical devices--Part 1: Evaluation and testing within a risk management process" and include the following:

- Use of surface area/extraction volume ratio (unless mass/extract volume ratio results in equivalent or higher amount of test sample)
- No dilutions of extract or test solutions, unless required for dose-dependent cytotoxicity studies
- No filtration/centrifugation
- No pH/osmolality adjustment
- Documentation of any color changes, turbidity or particles in the extract
- How representative portions are selected for testing, if the test system cannot accommodate all of the direct and indirect tissue contacting device components, to include documentation of what was excluded
- How extraction vehicle volume will be determined and documented for absorbent devices (e.g., spongy devices)

- How sample extraction ratios will be selected for devices having multiple components with different thicknesses
- How components with different types and durations of contact will be separated for sample preparation and testing
- Situations when pooled component samples (with same or different types or duration of tissue contact) will be allowed
- Inclusion of only tissue contacting components (unless procedure describes how inclusion of non-tissue contacting components will be addressed in determination of extraction ratios)
- Submersion of large devices completely in extraction vehicle
- How extractions will be conducted for devices containing fluid path components
- That the following types of devices are excluded for the ASCA Pilot: absorbable and in situ polymerizing devices, liquid devices, creams, gels, hydrogel devices, and devices containing nanomaterials.

7.4 Handling of test or calibration items
There are no additional specifications to those set forth in ISO/IEC 17025.

7.5 Technical records
There are no additional specifications to those set forth in ISO/IEC 17025.

7.6 Evaluation of measurement uncertainty
There are no additional specifications to those set forth in ISO/IEC 17025.

7.7 Ensuring the validity of results

To confirm the validity of the testing methods, any test-specified positive, negative, and/or reference controls allow for distinguishing between positive and negative responses. The testing laboratory agrees that pre-defined criteria for positive/negative/reference control values will be as follows:

- For cytotoxicity testing (per ISO 10993-5):
  - each positive control material replicate is ≥ Grade 3
  - each negative control material replicate is Grade 0
  - each vehicle control replicate is Grade 0
- For intracutaneous reactivity irritation testing:
  - each of five sodium chloride control sites in each animal at all timepoints is Grade 0
  - each of five oil control sites in each animal at all timepoints is ≤ Grade 1
- For primary skin (dermal) irritation testing, each sodium chloride and oil control site is Grade 0
- For guinea pig maximization sensitization testing (per ASTM F720):[11]

[11] ASTM F720-17: *Standard Practice for Testing Guinea Pigs for Contact Allergens: Guinea Pig Maximization Test*

- all sodium chloride and oil vehicle control animals have Grade 0 results at all sites
- the positive controls are run at least biannually (for each animal source) and each animal is at least one grade higher than concurrently run sodium chloride and oil vehicle controls in at least 8 out of 10 positive control animals (for strong sensitizers such as 0.1-0.5% dinitrochlorobenzene (DNCB) at induction and 0.05-0.1% DNCB at challenge)

- For closed patch sensitization testing:
  - all negative control animals (e.g., sodium chloride or oil vehicles or negative control materials) are Grade 0.
  - the positive controls are run at least biannually (for each animal source) and each animal is at least one Grade higher than concurrently run sodium chloride and oil vehicle controls in at least 8 out of 10 positive control animals (for strong sensitizers such as 0.1-0.5% DNCB at induction and 0.05-0.1% DNCB at challenge)
- For acute systemic toxicity testing, all sodium chloride and oil control animals result in no adverse clinical findings, no decrease in body weight > 10% per animal, and no deaths
- For material-mediated pyrogenicity testing there are no predefined criteria
- For hemolysis testing (per ASTM F756):
  - the positive control material mean hemolytic index is ≥ 5%
  - the negative control material mean hemolytic index is < 2%
- For complement activation testing using SC5b-9 (a product of the terminal pathway for complement activation),
  - the positive control meets one of the following criteria:
    - the mean value for the cobra venom factor positive control (if applicable) is at least 10X greater than both the mean values for the negative control material and the activated normal human serum, plasma, or whole blood, or
    - the positive material control (if applicable) is statistically significantly higher than both the negative control material and the activated normal human serum, plasma, or whole blood,
  - any kit-specific high and low controls meet the kit specifications.

7.8 Reporting of results

a) The testing laboratory agrees that it will have procedures to record all required information in ISO/IEC 17025 for each test conducted, including the following:
   - Test procedure(s) and test standard(s) used
   - Product or component(s) tested
   - Test equipment used for testing, measurement, or review (including the equipment's ratings and accuracies, unless otherwise readily available)
   - Date of the test(s). For example, periodic controls may have different test dates
   - Test report number, including revision number and amendment date, if applicable, and any related sub-contracted test report number(s)

- Names of the personnel performing the test(s) and the names of all supervisory personnel involved in the study and for biological studies, the signature of the study director and quality assurance unit personnel (i.e., per 21 CFR part 58, Good Laboratory Practices for Nonclinical Laboratory Studies, requirements)
- The test conditions as specified by the test standard, if applicable, (e.g., required voltage, power, temperature, or humidity for the test)
- Sample preparation:
  - images of device (or representative portion, if full device is not used) prior to and post sample preparation
  - use of subdivision/cutting
- Extraction conditions, if applicable:
  - extraction vehicle, time, temperature, and test article/vehicle ratio
  - storage time and temperature prior to application to the test system
  - images of vehicle post-extraction (color, cloudiness, presence of particulates)
- Sample manipulation:
  - filtration, centrifugation, dilution, pH adjustment, osmolality adjustment or other deviations from the sampling procedures
- Any deviations from the laboratory's ASCA accepted procedures as well as any amendments to the test report
- Test results to include:
  - opinions and interpretations included in a test report
  - all of the applicable data required by the laboratory's procedures; and
  - a statement that testing was conducted according to 21 CFR 58 Good Laboratory Practices for Nonclinical Laboratory Studies regulations[12]

b) The testing laboratory agrees that testing conducted by subcontractors will also comply with the above test report specifications, as applicable.
c) The testing laboratory agrees that the complete test report and an ASCA Summary Test Report will be submitted to the client at the end of testing activities

7.9 Complaints
There are no additional specifications than those set forth in ISO/IEC 17025.

7.10 Nonconforming work
There are no additional specifications than those set forth in ISO/IEC 17025.

7.11 Control of data and information management
There are no additional specifications than those set forth in ISO/IEC 17025.

ISO/IEC 17025 Section 8 ("Management system requirements")

[12] As discussed at the public workshop titled "Accreditation Scheme for Conformity Assessment of Medical Devices to Food and Drug Administration-Recognized Standards," biocompatibility testing conducted under the ASCA Pilot will be conducted in accordance with 21 CFR 58 Good Laboratory Practices for Nonclinical Laboratory Studies regulations.

8.1 Options

Regardless of the option selected (i.e., Option A or Option B), the testing laboratory agrees to maintain an Index of SOPs and any relevant ASCA test-related documents (e.g., SOPs, work instructions, master protocols, test-specific protocols, data collection worksheets, training information) applicable to any biological evaluation of medical device standards or test methods.

V. Premarket Submission Contents for FDA-Recognized Consensus Standards and Test Methods in the ASCA Pilot for Biocompatibility Testing of Medical Devices

FDA recommends that the following be included in any regulatory submission that contains biocompatibility testing conducted by an ASCA-accredited testing laboratory.

A. Cover Letter

FDA's recommendations regarding the content to be included in a cover letter for a premarket submission containing testing results from an ASCA-accredited testing laboratory are provided in FDA's guidance The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program.

B. Declaration of Conformity

Section IV.A. of FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices[13] recommends contents for a declaration of conformity (DOC) to an FDA-recognized consensus standard. For biocompatibility testing from an ASCA-accredited testing laboratory, FDA recommends the device manufacturer include the following additional items in the DOC:

- Date(s) the testing was conducted
- Location(s) where the testing was conducted
- Confirmation that the FDA-recognized consensus standards (and specific test methods) used during testing were within the laboratory's scope of *ASCA Accreditation* and not subject to any temporary labeling constraints as a result of a suspension of *ASCA Accreditation* at the time testing was conducted. If the relevant standard (and specific test method) was impacted by a suspension of *ASCA Accreditation*, the DOC should include an explanation of how this suspension may or may not affect the testing results.
- Limitations on the validity of the DOC:

[13] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices

- How the test article compares with the device provided in this premarket submission (including selection of "representative" devices/portions)[14]
- How any concerns communicated by the test lab were resolved
- How any observations and/or degradations during testing were resolved
- Whether any adverse or unusual findings as described in the list in Section V.C. occurred and, if so, rationale for acceptability

An example DOC is provided in Appendix A of this guidance. This example provides one approach to how a single DOC might contain testing to FDA-recognized consensus standards included and not included in a testing laboratory's scope of *ASCA Accreditation*.

C. Supplemental Documentation

An ASCA summary test report is recommended for all testing conducted under the ASCA Pilot. Example ASCA summary test reports are provided in Appendices B- J of this guidance. Note that the ASCA-accredited testing laboratory provides the ASCA summary test report to the device manufacturer who then includes it with its own DOC in a premarket submission to FDA. Depending on the information provided in the DOC or the ASCA summary test report, FDA may or may not need to review the complete test report for biocompatibility testing,[15] and the testing laboratory and/or device manufacturer may also be requested to provide a rationale to support a decision on a premarket submission.

During the ASCA Pilot, FDA generally will accept determinations from ASCA-accredited testing laboratories (i.e., test results) when the standard and test methods are within the testing laboratory's scope of *ASCA Accreditation* at the time of testing. Circumstances where FDA may request and review additional information related to testing from an ASCA-accredited testing laboratory are described in the bulleted points of Section XIII. A of the guidance titled The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program.

The ASCA Pilot processes and policies enhance confidence in testing results only when specific test methods and acceptance criteria are used. For example, FDA reviews a copy of the Index of SOPs and any relevant ASCA test-related documents (e.g., SOPs, work instructions, master protocols, test-specific protocols, data collection worksheets, training information) for testing laboratories that apply for a scope of *ASCA Accreditation* that includes biocompatibility testing. This review provides FDA an understanding of how testing is conducted, thereby providing confidence in the competence of ASCA-accredited testing laboratories. Depending on the specific device or intended use, deviations or amendments relative to the testing documentation submitted to FDA during the *ASCA Accreditation*

[14] Please see FDA's guidance Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" for considerations regarding the use of medical devices in their final finished form or a representative test article for biocompatibility testing."

[15] A complete test report for biocompatibility testing is described in Attachment E of FDA's guidance Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"

application process[16] may be appropriate. In such cases, FDA recommends a complete test report be included in the premarket submission. FDA also recommends a complete test report be included in the premarket submission for specific circumstances when (based on FDA's review experience) results may indicate a potential concern; these cases are noted below and in each example ASCA summary test report (*Refer to Appendices B-J*).

To allow FDA to determine if any additional information is needed, and whether the ASCA summary test report was insufficient for evaluation, a complete test report (in addition to the ASCA summary test report) is recommended for biocompatibility testing of medical devices in the cases outlined below.

- If test article was prepared per the ASCA Test Article Prep SOP specified on the ASCA summary test report (*Refer to Appendices B-J of this guidance*) with deviations/amendments (e.g., filtering, extract manipulation, pH adjustment)
- If extraction solvent, ratio, or conditions other than those specially called out in the example ASCA summary test report (*Refer to Appendices B-J of this guidance*) were used
- If there were any changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article
- If testing was conducted per the ASCA Test Method SOP specified on the ASCA summary test report (*Refer to Appendices B-J of this guidance*) and per 21 CFR 58 with deviations/amendments.
- For irritation- intracutaneous reactivity (ISO 10993-10) testing:
    - If the overall score differences between the test and control are greater than one (i.e., per ISO 10993-10:2010, Clause 6.4.7), or if there were non-zero results for any of the sodium chloride control sites in any animal or results greater than 1 for any of the oil control sites in any animal at any timepoint.
    - If adverse clinical findings or animal deaths occurred.
- For cytotoxicity – MEM Elution (ISO 10993-5) testing: if there were non-zero results for the test article, vehicle control or negative control, or if there were results less than 3 for the positive control at any timepoint.
- For dermal irritation (ISO 10993-10):
    - If direct contact was used and the test article was not the entire final finished device or a representative sample selection per the ASCA Test Article Prep SOP
    - If the primary irritation score is calculated using different timepoints besides 24hrs, 48hrs and 72hrs, if there were any non-zero test or control (e.g., direct contact control: gauze; extract test control: sodium chloride or oil) results at any time point.
    - If adverse clinical findings or animal deaths occurred.
- For guinea pig maximization sensitization (ISO 10993-10 and ASTM F720):

[16] Testing that includes deviations (and for which a DOC would not be appropriate) does not meet the criteria for inclusion in the ASCA Pilot as described in Section XII.B. of the guidance titled The Accreditation Scheme for Conformity Assessment (ASCA) Pilot Program.

    - If the Magnusson and Kligman grades of 1 or greater observed in the test group, provided grades of less than 1 are seen in corresponding sodium chloride or oil control animals (i.e., per ISO 10993-10:2010, Clause 7.5.6).
    - If differences in source, strain, treatment methods, or timing of the positive control occurred
    - If adverse clinical findings or animal deaths occurred.
- For closed patch sensitization (ISO 10993-10):
    - If direct contact was used and the test article was not the entire final finished device or a representative sample selection per the ASCA Test Article Prep SOP
    - If the Magnusson and Kligman grades of 1 or greater observed in the test group, provided grades of less than 1 are seen in negative control animals (i.e., per ISO 10993-10:2010, Clause 7.5.6), or the sodium chloride and oil vehicle controls are > Grade 0
    - If differences in source, strain, treatment methods, or timing of the positive control occurred
    - If adverse clinical findings or animal deaths occurred.
- For acute systemic toxicity (ISO 10993-11):
    - If any test or control animals died or had any adverse clinical findings
    - If any test animals had a body weight loss greater than 10%.
- For material-mediated pyrogenicity (ISO 10993-11 and USP 151):
    - If any rabbit has a baseline temperature exceeding 39.8°C, or if any rabbit has a temperature rise ≥0.5°C
    - If adverse clinical findings or animal deaths occurred.
- For direct and indirect hemolysis (ISO 10993-4 and ASTM F756):
    - If direct contact was used and the test article was not the entire final finished device or a representative sample selection per the ASCA Test Article Prep SOP
    - If direct contact was used and a diluent other than Magnesium and Calcium Free PBS was used (i.e., per ASTM F756-17, Section 3.1.10)
    - If direct contact was used and an exposure ratio other than those specially called out in the example ASCA summary test report (*Refer to Appendix I of this guidance*) was used (i.e., per ASTM F756-17, Section 9.2.1)
    - If negative and positive controls did not perform as expected, the negative control, test article, and blank had absorbance values of 0.000 for all replicates, or test article scores of ≥2% Hemolytic Index.
- For complement activation (ISO 10993-4):
    - If the test article was not the entire final finished device or a representative sample selection per the ASCA Test Article Prep SOP
    - If a test medium other than those specifically called out in the example ASCA summary test report (*Refer to Appendix J of this guidance*) was used
    - If exposure ratio or conditions other than those specially called out in the example ASCA summary test report (*Refer to Appendix J of this guidance*) were used

- If test medium, negative, positive, and comparator controls did not perform as expected, or there was a statistically significant increase in SC5b-9 for test article compared to negative or comparator controls.

VI. Paperwork Reduction Act of 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521).

The time required to complete this information collection is estimated[17] to average 95 hours per response for accreditation bodies and 47 hours for testing laboratories. Send comments regarding this burden estimate or suggestions for reducing this burden to:

FDA PRA Staff,
Office of Operations,
Food and Drug Administration,
PRAStaff@fda.hhs.gov

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0889 (expires 06-30-2023).

[17] Rounded to the nearest whole number.

Appendix A: Example ASCA Declaration of Conformity (DOC) for Biological Evaluation of Medical Devices Standards in the ASCA Pilot

Note: This example is intended to illustrate elements of the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices *that the device manufacturer may submit as part of its premarket submission.*

Responsible Party
Name of entity responsible for DOC: _____
Address of entity responsible for DOC: _____

Product/Device Identification

All identifying information for the product/device including (e.g., product code(s), device marketing name(s), model number(s), etc.).

Statement of Conformity
☐ The test results demonstrate that the device is in conformity with the standard(s) listed below:[18]

1. Title of Standard: (e.g., *ISO 10993-10 Third edition 2010-08-01 Biological evaluation of medical devices – Part 10: Tests for irritation and skin sensitization*)-___
   - FDA Recognition #: *(e.g., 2-174)*
   - Options Selected
     - ☐ Standard included no options
     - ☐ Standard included options

List of options selected in standard (e.g., Clause 7.3 Guinea pig assays for detection of skin sensitization). No information is needed in this section if testing is from an ASCA-accredited test laboratory; instead, this section may reference the ASCA summary test report provided as supplementary documentation.
   - Testing Laboratory Name: (*e.g., Testing Laboratory ABC)*
   - ASCA Testing Laboratory Identification Number (as applicable): (*e.g., ASCA001)*
   - Testing Location(s): (*e.g., 1234 Example Road, Silver Spring, MD 20993)*

[18] See section 514(c)(3)(A)(i) of the FD&C Act, cited in Section IV.A.(3)(f) of FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Device.

- Testing Date(s): (*e.g., Sep 1, 2020 – Sep 15, 2020)*_____
- *ASCA Accreditation* Status on the Date(s) of Testing:
  ☐ Standard (and particular test method) was not in testing laboratory's scope of *ASCA Accreditation*
  ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*;_____
    ☐ *ASCA Accreditation* was not suspended
    ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results, including date(s) of suspension.

- Supplemental Documentation (*see Section V.C. of this guidance for specific recommendations*):
  ☐ Supplementary documentation is not included
  ☐ Supplementary documentation is included at the following location within the submission, and I have checked that there are no differences regarding protocol and data between the complete test report and the supplemental documentation: (*e.g., Appendix A of this premarket submission*)_____

<Repeat for each standard in DOC>

Limitations on Validity of DOC

Description of any limitation on the validity of the DOC (e.g., how long the declaration is valid, what was tested, or concessions made about the testing outcomes). For testing from an ASCA-accredited test laboratory, this should include, at a minimum:

- *Information on how the test article compares with the device provided in this premarket submission[19] (including, selection of "representative" devices/portions) can be found at the following location in this premarket submission: (e.g., Section V. pages 45-50)*
- *Information on how any concerns communicated by the test lab were resolved can be found at the following location in this premarket submission: (e.g., Appendix D of this premarket submission)*
- *Information on how any observations and/or degradations during testing were resolved can be found at the following location in this premarket submission: (e.g., Appendix D of this premarket submission)*
- *A statement that the device/test article does not require customized sample preparation and/or testing methodologies, or any absorbable or in situ polymerizing devices, liquid devices, creams, gels, hydrogel devices, and devices containing nanomaterials, as these types of materials are not eligible for biocompatibility testing under the ASCA Pilot*

Signature

Printed name: _____
Function within entity responsible for DOC: _____

_____
Signature Date

[19] Please see FDA's guidance Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" for considerations regarding the use of medical devices in their final finished form or a representative test article for biocompatibility testing.

Appendix B: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Irritation – Intracutaneous Reactivity (ISO 10993-10)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[20]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: ***[****ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[21] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

☐ For devices that contain fluid paths only, the Test Article was prepared using only the fluid path for extraction

Extraction Solvent:

☐ 0.9% Sodium Chloride (SC)

[20] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[21] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

- ☐ Cotton Seed Oil (CSO)/Sesame Oil (SO)
- ☐ Other:[22] *[DESCRIBE]*

Extraction Ratio:

- ☐ 6cm^2/ml (<0.5mm thick)
- ☐ 3cm^2/ml (0.5-1.0mm thick or molded items > 1.0mm)
- ☐ 1.25cm^2/ml (elastomers > 1.0mm thick)
- ☐ Other:[23] *[DESCRIBE]*

Extraction Conditions:

- ☐ 37°C, 72 h
- ☐ 50°C, 72 h
- ☐ 70°C, 24 h
- ☐ 121°C, 1 h
- ☐ Other:[24] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[25]

- ☐ Complete fill with agitation
- ☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
- ☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
- ☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[26]

ASCA Test Method SOP #: *[ASCAIntracut(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

[22] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[23] *Ibid*

[24] *Ibid*

[25] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report is requested in addition to the ASCA Summary Test Report.

[26] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[27]

Description of deviations/amendments

Results:[28]

	Test Article	24 hr Results	48 hr Results	72 hr Results	Conclusions
Animal 1	SC Test	ER^: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	Performed as expected
	SC Control	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	Performed as expected
Animal 2	SC Test	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	Performed as expected
	SC Control	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	Performed as expected
Animal 3	SC Test	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	Performed as expected
	SC Control	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	ER: 0/0/0/0/0 ED: 0/0/0/0/0	Performed as expected
Animal 1	SO Test	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/0/1/1/1 ED: 0/0/0/0/0	ER: 1/0/1/1/1 ED: 0/0/0/0/0	Performed as expected
	SO Control	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/1/0/0/1 ED: 0/0/0/0/0	Performed as expected
Animal 2	SO Test	ER: 1/1/1/1/1 ED: 0/0/1/0/0	ER: 1/1/1/1/0 ED: 0/0/1/0/0	ER: 1/1/1/1/0 ED: 0/0/0/0/0	Performed as expected
	SO Control	ER: 1/1/1/1/0 ED: 0/0/1/0/0	ER: 1/1/1/0/1 ED: 0/0/0/0/0	ER: 1/1/0/0/0 ED: 0/0/0/0/0	Performed as expected
Animal 3	SO Test	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/1/1/1/1 ED: 0/0/0/0/0	Performed as expected
	SO Control	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/1/1/1/1 ED: 0/0/0/0/0	ER: 1/1/1/1/1 ED: 0/0/0/0/0	Performed as expected

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

^ER = erythema grade; ED = edema grade

[27] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not need to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[28] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot, if the overall score differences between the test and control are greater than one (i.e., per ISO 10993-10:2010, Clause 6.4.7), or if there were non-zero results for any of the sodium chloride control sites in any animal, or results greater than 1 for any of the oil control sites in any animal at any timepoint.

Extract	Overall Test Group Mean	Overall Control Group Mean	Overall Mean Difference (Test – Control)	Conclusion
SC	0.0	0.0	0.0	Non-Irritant
SO	1.0	0.9	0.1	Non-Irritant

☐ There were no adverse clinical findings or animal deaths; or
☐ The following adverse clinical findings or animal deaths occurred:[29]

Description of adverse clinical findings or animal deaths

I confirm that:
☐ The above summary information includes all original and any retest data; and
☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

[29] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Appendix C: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Cytotoxicity – MEM Elution (ISO 10993-5)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[30]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: *[ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[31] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Extraction Solvent:

- ☐ MEM with 5-10% animal serum
- ☐ Other:[32] *[DESCRIBE]*

[30] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[31] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[32] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test

Extraction Ratio:

- ☐ $6cm^2/ml$ (<0.5mm thick)
- ☐ $3cm^2/ml$ (0.5-1.0mm thick or molded items > 1.0mm)
- ☐ $1.25cm^2/ml$ (elastomers > 1.0mm thick)
- ☐ Other:[33] *[DESCRIBE]*

Extraction Conditions:

- ☐ 37°C, 24 h
- ☐ 37°C, 72 h
- ☐ 50°C, 72 h
- ☐ 70°C, 24 h
- ☐ 121°C, 1 h
- ☐ Other:[34] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[35]

- ☐ Complete fill with agitation
- ☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
- ☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
- ☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[36]

ASCA Test Method SOP #: *[######-ASCACytotox(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[37]

report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[33] *Ibid*

[34] *Ibid*

[35] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.

[36] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[37] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Description of deviations/amendments

Results:[38]

	24 hr Results (optional)	**48 hr Results**	**72 hr Results (implants)**	**Conclusion**
Vehicle Control	Grade 0/0/0	Grade 0/0/0	Grade 0/0/0	Performed as expected
Negative Control HDPE	Grade 0/0/0	Grade 0/0/0	Grade 0/0/0	Performed as expected
Positive Control Latex	Grade 3/3/3	Grade 4/4/4*	Grade 4/4/4	Performed as expected
Test Article Extract (100% neat)	Grade 0/0/0	Grade 0/0/0	Grade 0/0/0	Non-cytotoxic
[INSERT ROWS FOR ANY ADDITIONAL TEST ARTICLE DILUTION/RETEST DATA]				

*based on prior results (once Grade 4 results are observed, subsequent assessment is not necessary for cytotoxicity)

I confirm that:
☐ The above summary information includes all original and any retest data; and
☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

Name: [TYPED NAME, POSITION] Date

[38] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if there were non-zero results for the test article, vehicle control or negative control, or if there were results less than 3 for the positive control at any timepoint.

Appendix D: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Dermal Irritation (ISO 10993-10)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[39]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: ***[****ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[40] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Direct contact

Test article:

- ☐ Entire final finished device
- ☐ Representative sample selection per SOP

[39] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[40] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also request to provide a rationale to support a regulatory decision.

☐ Other:[41] *[DESCRIBE]*

Extract testing

Extraction Solvent:

☐ 0.9% Sodium Chloride (SC)
☐ Cotton Seed Oil (CSO)/Sesame Oil (SO)
☐ Other:[42] *[DESCRIBE]*

Extraction Ratio:

☐ $6cm^2$/ml (<0.5mm thick)
☐ $3cm^2$/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ $1.25cm^2$/ml (elastomers > 1.0mm thick)
☐ Other:[43] *[DESCRIBE]*

Extraction Conditions:

☐ 37°C, 72 h
☐ 50°C, 72 h
☐ 70°C, 24 h
☐ 121°C, 1 h
☐ Other:[44] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[45]

☐ Complete fill with agitation
☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[46]

---

[41] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[42] *Ibid*
[43] *Ibid*
[44] *Ibid*
[45] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.
[46] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

ASCA Test Method SOP #: *[ASCADermalIrri(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[47]

Description of deviations/amendments

Results:[48]

Table 1 Summary of Scores for Dermal Irritation*

Animal Number	Test/Control Article Sites	Score @ 1hr		Score @ 24hr		Score @ 48hr		Score @ 72hr	
		ER	ED	ER	ED	ER	ED	ER	ED
1	Test Site-1	0	0	0	0	0	0	0	0
	Test Site-2	1	0	0	0	0	0	0	0
	Control Site-1	0	0	0	0	0	0	0	0
	Control Site-2	0	0	0	0	0	0	0	0
2	Test Site-1	0	0	0	0	0	0	0	0
	Test Site-2	0	0	0	0	0	0	0	0
	Control Site-1	0	0	0	0	0	0	0	0
	Control Site-2	0	0	0	0	0	0	0	0
3	Test Site-1	0	0	0	0	0	0	0	0
	Test Site-2	0	0	0	0	0	0	0	0
	Control Site-1	0	0	0	0	0	0	0	0
	Control Site-2	0	0	0	0	0	0	0	0

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

**For extract-based tests: animal data[49] for both polar and nonpolar test extracts and corresponding vehicle controls should be reported.*

[47] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[48] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if the primary irritation score is calculated using different timepoints besides 24h, 48h and 72h, if there were any non-zero test or control (e.g., direct contact control: gauze; extract test control: sodium chloride or oil) results at any time point.

[49] We support the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method. However, these alternative methods would not be eligible for the ASCA pilot. See generally: https://www.fda.gov/science-research/advancing-regulatory-science/vi-modernizing-safety-testing

^ER = erythema grade; ED = edema grade

Table 2 Summary of Primary Irritation Index*

Animal Number	Test Score Average	-	Control Score Average	Individual Primary Irritation Score	Combined Primary Irritation Score (CPIS)	Primary Irritation Index (CPIS÷3)	Response Category	Conclusion
1	0.0	-	0.0	0.0	0.0	0.0	Negligible	Non-irritant
2	0.0	-	0.0	0.0				
3	0.0	-	0.0	0.0				

**For extract-based tests: animal data for both polar and nonpolar test extracts and corresponding vehicle controls should be reported.*

☐ There were no adverse clinical findings or animal deaths; or
☐ The following adverse clinical findings or animal deaths occurred:[50]

Description of adverse clinical findings or animal deaths

I confirm that:
☐ The above summary information includes all original and any retest data; and
☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

[50] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Appendix E: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Guinea Pig Maximization Sensitization (ISO 10993-10)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[51]
   ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
      ☐ *ASCA Accreditation* was not suspended
      ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: ***[****ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or
☐ Test Article was prepared per the above protocol, with the following deviations/amendments[52] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Extraction Solvent:

☐ 0.9% Sodium Chloride (SC)
☐ Cotton Seed Oil (CSO)/Sesame Oil (SO)

[51] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[52] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

☐ Other:[53] *[DESCRIBE]*

Extraction Ratio:

☐ 6cm^2/ml (<0.5mm thick)
☐ 3cm^2/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ 1.25cm^2/ml (elastomers > 1.0mm thick)
☐ Other:[54] *[DESCRIBE]*

Extraction Conditions:

☐ 37°C, 72 h
☐ 50°C, 72 h
☐ 70°C, 24 h
☐ 121°C, 1 h
☐ Other:[55] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[56]

☐ Complete fill with agitation
☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[57]

[53] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also request to provide a rationale to support a regulatory decision.
[54] *Ibid*
[55] *Ibid*
[56] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.
[57] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

ASCA Test Method SOP #: *[ASCAMaximizationSensi(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[58]

Description of deviations/amendments

[58] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Results:[59]

Table 1 Summary of Scores for Sensitization

Group	Animal Number	24hrs		48hrs		Sensitization Frequency	Conclusion
		Control Site	Test Site	Control Site	Test Site		
SC Test	**1**	0	0	0	0	0%	Non-sensitizer
	2	0	0	0	0		
	3	0	0	0	0		
	4	0	0	0	0		
	5	0	0	0	0		
	6	0	0	0	0		
	7	0	0	0	0		
	8	0	0	0	0		
	9	0	0	0	0		
	10	0	0	0	0		
SC Control	**1**	0	0	0	0	0%	Performed as expected
	2	0	0	0	0		
	3	0	0	0	0		
	4	0	0	0	0		
	5	0	0	0	0		
SO Test	**1**	0	0	0	0	0%	Non-sensitizer
	2	0	0	0	0		
	3	0	0	0	0		
	4	0	0	0	0		
	5	0	0	0	0		
	6	0	0	0	0		
	7	0	0	0	0		
	8	0	0	0	0		
	9	0	0	0	0		
	10	0	0	0	0		
SO Control	**1**	0	0	0	0	0%	Performed as expected
	2	0	0	0	0		
	3	0	0	0	0		
	4	0	0	0	0		
	5	0	0	0	0		
	1	0	2	0	2	100%	
	2	0	2	0	1		

[59] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot, if the Magnusson and Kligman grades of 1 or greater observed in the test group, provided grades of less than 1 are seen in control animals (i.e., per ISO 10993-10:2010, Clause 7.5.6).

Dinitrochlorobenzene (DNCB) Positive Control*	**3**	0	2	0	3		Performed as expected
	4	0	2	0	2		
	5	0	2	0	2		

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

***Periodic/concurrent positive control study**

☐ Positive control induction concentration: *[DESCRIBE]*
☐ Positive control challenge concentration: *[DESCRIBE]*
☐ The same source, strain, and treatment methods used for positive control testing and done within 3 months of test article test date
☐ The following differences in source, strain, treatment methods or timing of the positive control occurred:[60]

Description of differences in source, strain, treatment methods, or timing of the positive control.

☐ There were no adverse clinical findings or animal deaths; or
☐ The following adverse clinical findings or animal deaths occurred: [61]

Description of adverse clinical findings or animal deaths.

I confirm that:
☐ The above summary information includes all original and any retest data; and
☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

[60] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[61] *Ibid*

Appendix F: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Closed Patch Sensitization (ISO 10993-10)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[62]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: ***[****ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[63] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Direct contact

Test article:

- ☐ Entire final finished device
- ☐ Representative sample selection per SOP

[62] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[63] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

☐ Other:[64] *[DESCRIBE]*

Extract testing

Extraction Solvent:

☐ 0.9% Sodium Chloride (SC)
☐ Cotton Seed Oil (CSO)/Sesame Oil (SO)
☐ Other:[65] *[DESCRIBE]*

Extraction Ratio:

☐ $6cm^2$/ml (<0.5mm thick)
☐ $3cm^2$/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ $1.25cm^2$/ml (elastomers > 1.0mm thick)
☐ Other:[66] *[DESCRIBE]*

Extraction Conditions:

☐ 37°C, 72 h
☐ 50°C, 72 h
☐ 70°C, 24 h
☐ 121°C, 1 h
☐ Other:[67] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[68]

☐ Complete fill with agitation
☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[69]

ASCA Test Method SOP #: *[ASCAPatchSens(date/version)]*

[64] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[65] *Ibid*
[66] *Ibid*
[67] *Ibid*
[68] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.
[69] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[70]

Description of deviations/amendments

Results:[71]

Table 1 Summary of Scores for Sensitization*

Group	Animal Number	24hrs		48hrs		Sensitization Frequency	Conclusion
		Control Site	Test Site	Control Site	Test Site		
Test	**1**	0	0	0	0	0%	Non-sensitizer
	2	0	0	0	0		
	3	0	0	0	0		
	4	0	0	0	0		
	5	0	0	0	0		
	6	0	0	0	0		
	7	0	0	0	0		
	8	0	0	0	0		
	9	0	0	0	0		
	10	0	0	0	0		
Gauze Negative Control	**1**	0	0	0	0	0%	Performed as expected
	2	0	0	0	0		
	3	0	0	0	0		
	4	0	0	0	0		
	5	0	0	0	0		
Dinitrochlorobenzene (DNCB) Positive Control**	**1**	0	2	0	2	100%	Performed as expected
	2	0	2	0	1		
	3	0	2	0	3		
	4	0	2	0	2		
	5	0	2	0	2		

[70] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[71] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if the Magnusson and Kligman grades of 1 or greater observed in the test group, provided grades of less than 1 are seen in negative control animals (i.e., per ISO 10993-10:2010, Clause 7.5.6), or the sodium chloride and oil vehicle controls are > Grade 0.

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

**For extract-based tests: animal data for both polar and nonpolar test extracts and corresponding vehicle controls should be reported.*

****Periodic/concurrent positive control study**

☐ Positive control induction concentration: *[DESCRIBE]*
☐ Positive control challenge concentration: *[DESCRIBE]*
☐ The same source, strain, and treatment methods used for positive control testing and done within 3 months of test article test date
☐ The following differences in source, strain, treatment methods or timing of the positive control occurred: [72]

Description of differences in source, strain, treatment methods, or timing of the positive control

☐ There were no adverse clinical findings or animal deaths; or
☐ The following adverse clinical findings or animal deaths occurred:[73]

Description of adverse clinical findings or animal deaths

I confirm that:
☐ The above summary information includes all original and any retest data; and
☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

[72] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[73] *Ibid*

Appendix G: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Acute Systemic Toxicity (ISO 10993-11)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[74]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: *[ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[75] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Extraction Solvent:

- ☐ 0.9% Sodium Chloride (SC)
- ☐ Cotton Seed Oil (CSO)/Sesame Oil (SO)
- ☐ Other: [76] *[DESCRIBE]*

[74] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[75] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Extraction Ratio:

- ☐ $6cm^2/ml$ (<0.5mm thick)
- ☐ $3cm^2/ml$ (0.5-1.0mm thick or molded items > 1.0mm)
- ☐ $1.25cm^2/ml$ (elastomers > 1.0mm thick)
- ☐ Other:[77] *[DESCRIBE]*

Extraction Conditions:

- ☐ 37°C, 72 h
- ☐ 50°C, 72 h
- ☐ 70°C, 24 h
- ☐ 121°C, 1 h
- ☐ Other:[78] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[79]

- ☐ Complete fill with agitation
- ☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
- ☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
- ☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[80]

ASCA Test Method SOP #: *[ASCAAcuteTox(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[81]

---

[77] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[78] *Ibid*

[79] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.

[80] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[81] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Description of deviations/amendments

Results:[82]

Table 1 Summary of Test Results[83]

Extract	Animal Number	Body Weight (g)				Weight Change	Conclusion (Based on Body Weight and Clinical Findings)
		Day 0	Day 1	Day 2	Day 3		
SC Test	**1**	20.4	20.8	21.1	21.7	1.3	No acute systemic toxicity
	2	19.6	20.4	20.3	21.7	2.1	No acute systemic toxicity
	3	19.6	19.9	20.1	20.7	1.1	No acute systemic toxicity
	4	20.4	19.8	20.3	21.1	0.7	No acute systemic toxicity
	5	17.9	18.6	19.0	19.7	1.8	No acute systemic toxicity
SC Control	**1**	17.9	19.9	19.8	20.4	2.5	Performed as expected
	2	19.8	20.0	20.9	22.3	2.5	Performed as expected
	3	19.9	20.3	20.8	21.4	1.5	Performed as expected
	4	17.9	17.8	17.9	18.6	0.7	Performed as expected
	5	22.1	22.9	23.1	24.3	2.2	Performed as expected
SO Test	**1**	22.2	22.9	22.8	23.4	1.2	Not systemically toxic
	2	20.2	21.3	21.4	21.8	1.6	Not systemically toxic
	3	19.0	19.2	19.3	20.2	1.2	Not systemically toxic
	4	18.5	19.8	20.5	21.6	3.1	Not systemically toxic
	5	19.4	202.2	19.8	20.0	0.6	Not systemically toxic
SO Control	**1**	19.7	20.2	20.5	21.9	2.2	Not systemically toxic
	2	19.4	19.9	19.7	20.0	0.6	Not systemically toxic
	3	21.2	21.7	22.2	23.6	2.4	Not systemically toxic
	4	20.9	21.7	22.0	23.1	2.2	Not systemically toxic
	5	20.3	21.1	21.6	23.4	3.1	Not systemically toxic

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

☐ There were no adverse clinical findings or animal deaths; or
☐ The following adverse clinical findings or animal deaths occurred:[84]

[82] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if controls did not perform as expected, any animals were found dead or were euthanized, behavior such as convulsions or prostration occurred in any animals, or a body weight loss greater than 10 % occurred in any animals.
[83] This is an example of how data from an acute systemic toxicity test could be presented.
[84] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Description of adverse clinical findings or animal deaths

I confirm that:
☐ The above summary information includes all original and any retest data; and
☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

Appendix H: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Material-Mediated Pyrogenicity (ISO 10993-11 and USP 151)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[85]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: *[ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[86] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Extraction Solvent:

☐ 0.9% Sodium Chloride (SC)

☐ Other:[87] *[DESCRIBE]*

[85] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[86] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[87] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test

Extraction Ratio:

- ☐ $6cm^2/ml$ (<0.5mm thick)
- ☐ $3cm^2/ml$ (0.5-1.0mm thick or molded items > 1.0mm)
- ☐ $1.25cm^2/ml$ (elastomers > 1.0mm thick)
- ☐ Other:[88] *[DESCRIBE]*

Extraction Conditions:

- ☐ 37°C, 72 h
- ☐ 50°C, 72 h
- ☐ 70°C, 24 h
- ☐ 121°C, 1 h
- ☐ Other:[89] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[90]

- ☐ Complete fill with agitation
- ☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
- ☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
- ☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.

☐ There were changes in color/ turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[91]

report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[88] *Ibid*

[89] *Ibid*

[90] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.

[91] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

ASCA Test Method SOP #: *[ASCAPyrogenicity(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[92]

Description of deviations/amendments

Results:[93]

Table 1 Pyrogen Test Data[94]

Animal Number	Baseline Temp (°C)	1.0hr Temp (°C)	1.5 hr Temp (°C)	2.0 hr Temp (°C)	2.5 hr Temp (°C)	3.0 hr Temp (°C)	Temp Increase (°C)	Conclusion
1 (test)	39.0	39.1	39.1	38.9	38.8	39.1	0.1	Non-pyrogenic
2 (test)	39.3	39.3	39.1	38.8	39.1	39.1	0.0	Non-pyrogenic
3 (test)	39.0	38.7	38.8	39.1	39.4	39.4	0.4	Non-pyrogenic

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

☐ There were no adverse clinical findings or animal deaths; or

☐ The following adverse clinical findings or animal deaths occurred:[95]

Description of adverse clinical findings or animal deaths

I confirm that:

☐ The above summary information includes all original and any retest data; and

☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

[92] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[93] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if any rabbit has a baseline temperature exceeding 39.8°C or if any rabbit has a temperature rise ≥0.5°C.

[94] This is an example of how data from a material-mediated pyrogenicity test could be presented.

[95] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Name: [TYPED NAME POSITION] Date

Appendix I: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Direct and Indirect Hemolysis (ISO 10993-4 and ASTM F756)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[96]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: ***[****ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[97] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Extract testing

Extraction Solvent:

☐ Magnesium and Calcium Free PBS

[96] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[97] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

☐ Other:[98] *[DESCRIBE]*

Extraction Ratio:

☐ 6cm^2/ml (<0.5mm thick)
☐ 3cm^2/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ 1.25cm^2/ml (elastomers > 1.0mm thick)
☐ Other:[99] *[DESCRIBE]*

Extraction Conditions:

☐ 37°C, 72 h
☐ 50°C, 72 h
☐ 70°C, 24 h
☐ 121°C, 1 h
☐ Other:[100] *[DESCRIBE]*

Fluid Path Extractions:

☐ For fluid path devices or components (where fluids contact the channels in the device or component, and then the fluid enters the body), the extraction was conducted using protocols specific to fluid path, with the following approach:[101]

☐ Complete fill with agitation
☐ Partial fill with agitation (ISO 10993-12 surface/volume ratio)
☐ Partial fill with agitation (other surface/volume ratio): [DESCRIBE RATIO USED]
☐ Other: [SUMMARIZE APPROACH]

☐ The test article and extract DID NOT change color, and the extract DID NOT appear turbid or have particles.
☐ There were changes in color/turbidity or particles in the test article and/or extract OR there was swelling/degradation of the test article.[102]

Direct Contact

Test article:

☐ Entire final finished device
☐ Representative sample selection per SOP
☐ Other:[103] *[DESCRIBE]*

Diluent:

☐ Magnesium and Calcium Free PBS

---

[98] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[99] *Ibid*
[100] *Ibid*
[101] The applicability of various approaches (e.g., partial fill versus complete fill) for a particular device may impact whether or not a complete test report should be included with the ASCA Summary Test Report.
[102] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[103] *Ibid*

☐ Other:[104] *[DESCRIBE]*

Exposure Ratio:

☐ $6cm^2$/ml (<0.5mm thick)
☐ $3cm^2$/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ Other:[105] *[DESCRIBE]*

☐ The test article and supernatant DID NOT change color, and the supernatant DID NOT appear turbid or have particles.
☐ There were changes in color/turbidity or particles in the supernatant OR there was swelling/degradation of the test article.[106]

ASCA Test Method SOP #: *[ASCAHemolysis(date/version)]*
☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or
☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments: [107]

Description of deviations/amendments

[104] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[105] *Ibid*
[106] *Ibid*
[107] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

Results:[108]

Table 1 Hemolysis test results[109]

Extract Hemolysis									
Sample	**Absorbance**			**Blank corrected % hemolysis**			**Mean Blank Corrected Hemolysis (%)**	**Hemolytic Index (%)**	**Conclusions**
	Replicate #1	**Replicate #2**	**Replicate #3**	**Replicate #1**	**Replicate #2**	**Replicate #3**			
Blank	0.0022	0.0019	0.0026	-0.01	-0.08	0.09	0.00	-	Performed as expected
Negative Control	0.0020	0.0018	0.0019	-0.06	-0.11	-0.08	-0.08	-	Performed as expected
Positive Control	0.3233	0.3258	0.3261	79.68	80.30	80.37	80.11	80.20	Performed as expected
Test	0.0019	0.0015	0.0015	-0.08	-0.18	-0.18	-0.15	-0.07	Non-hemolytic
Direct Hemolysis									
Sample	**Absorbance**			**Blank corrected % hemolysis**			**Mean Blank Corrected Hemolysis (%)**	**Hemolytic Index (%)**	**Conclusions**
	Replicate #1	**Replicate #2**	**Replicate #3**	**Replicate #1**	**Replicate #2**	**Replicate #3**			

[108] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if negative and positive controls did not perform as expected, the negative control, test article, and blank had absorbance values of 0.000 for all replicates, or test article scores of ≥2% HI.
[109] This is an example of how data from a hemolysis test could be presented.

Blank	0.0057	0.0059	0.0051	0.03	0.08	-0.12	0.00	-	Performed as expected
Negative Control	0.0074	0.0084	0.0103	0.46	0.71	1.18	0.78	-	Performed as expected
Positive Control	0.3732	0.3736	0.3752	91.99	92.09	92.49	92.19	91.41	Performed as expected
Test	0.0096	0.0091	0.0089	1.01	0.88	0.83	0.91	0.13	Non-hemolytic

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

I confirm that:

☐ The above summary information includes all original and any retest data; and

☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date

Appendix J: Example ASCA Summary Test Report for Biocompatibility Testing of Medical Devices: Complement Activation (ISO 10993-4)

Note: This example is intended to illustrate the supplemental documentation that would accompany the Declaration of Conformity per FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices. *The ASCA summary test report is provided by the testing laboratory to the device manufacturer.*

Administrative Information

1. Testing Laboratory Name:
2. ASCA Testing Laboratory Identification Number:
3. Testing Location(s):
4. Testing Date(s):
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☐ Standard (and particular test method) was *NOT* in testing laboratory's scope of *ASCA Accreditation*[110]
   - ☐ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☐ *ASCA Accreditation* was not suspended
     - ☐ *ASCA Accreditation* was suspended

Description of reasons for suspension and their impact on testing results.

ASCA Test Article Prep SOP#: ***[****ASCATAPrep(date/version)]*

☐ Test Article was prepared per the above protocol (no deviations/amendments); or

☐ Test Article was prepared per the above protocol, with the following deviations/amendments[111] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Test article:

- ☐ Entire final finished device
- ☐ Representative sample selection per SOP

[110] See FDA's guidance Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices for information regarding supplemental documentation necessary to support FDA-recognized consensus standards that are not in a testing laboratory's scope of *ASCA Accreditation*.

[111] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

☐ Other: [112]*[DESCRIBE]*

Test Medium:

☐ Normal Human Serum
☐ Human Plasma
☐ Whole Blood
☐ Other:[113]*[DESCRIBE]*

Exposure Ratio:

☐ 6cm^2/ml (<0.5mm thick)
☐ 3cm^2/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ Other:[114] *[DESCRIBE]*

Exposure Conditions:

☐ 37°C for 60-90 min
☐ Other:[115] *[DESCRIBE]*

☐ The test article and supernatant DID NOT change color, and the supernatant DID NOT appear turbid or have particles.
☐ There were changes in color/turbidity or particles in the supernatant OR there was swelling/degradation of the test article.[116]

[112] In this situation, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.
[113] *Ibid*
[114] *Ibid*
[115] *Ibid*
[116] *Ibid*

ASCA Test Method SOP #: *[ASCAComplement(date/version)]*

☐ Test was conducted per the above protocol (no deviations/amendments) and 21 CFR 58; or

☐ Test was conducted per the above protocol and 21 CFR 58, with the following deviations/amendments:[117]

Description of deviations/amendments

Results:[118]

Table 1 SC5b-9 Protein Concentration (ng/mL)[119]

Samples	Dilution	Concentration (ng/mL)					
		Replicate #1	Replicate #2	Replicate #3	Mean	Std	Conclusion
Test Article	1:160	208	216	212	212	3.8	Not a complement activator*
Test Medium Control	1:160	205	207	208	207	1.5	Performed as expected
Negative Control Material	1:160	206	205	204	205	1.1	Performed as expected
Positive Control Material[120]	1:160	683	693	688	688	4.8	Performed as expected
Cobra Venom Factor Positive Control[121]	1:8000	10326	10567	10519	10471	127	Performed as expected
US marketed comparator (optional)	1:160	210	215	223	216	6.6	Performed as expected

[INSERT ROWS FOR ANY ADDITIONAL REPEAT TEST DATA]

*not statistically different from negative or comparator controls

[117] Since deviations/amendments were noted, the complete test report should be included with ASCA Summary Test Report during the ASCA Pilot (depending on the information provided, FDA may or may not request to review the complete test report). Test Laboratory/Manufacturer may also be requested to provide a rationale to support a regulatory decision.

[118] The complete test report should be included with ASCA Summary Test Report during the ASCA Pilot if test medium, negative, positive, and comparator controls did not perform as expected, or there was a statistically significant increase in SC5b-9 for test article compared to negative or comparator controls.

[119] This is an example of how data from a complement activation test could be presented.

[120] Depending on the positive control used, this row may be relevant.

[121] *Ibid*

I confirm that:

☐ The above summary information includes all original and any retest data; and

☐ I have checked that there are no differences between the complete test report and this ASCA summary test report.

Name: [TYPED NAME POSITION] Date