U.S. FOOD & DRUG ADMINISTRATION

Streamlining Conformity Assessment: Putting Standards to Work

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Scott A. Colburn

Director

Standards and Conformity Assessment Program

Division of All Hazards Response, Science and Strategic Partnerships (DARSS)

Office of Strategic Partnerships and Technology Innovation (OST)

Center for Devices and Radiological Health

U.S. Food and Drug Administration

Standards: Regulatory Science's Ultimate Weapon

Learning Objectives

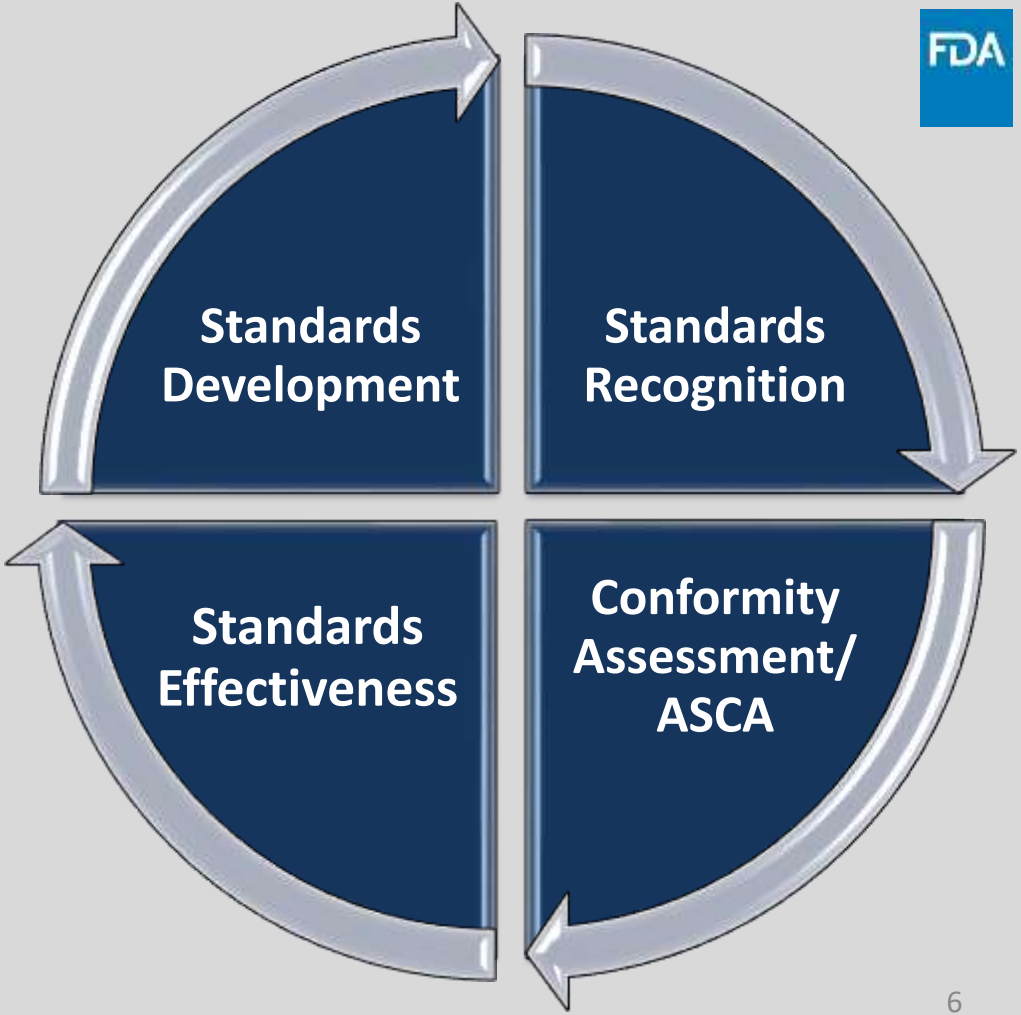
- Explain the value of standards in device review
- Describe how S-CAP advances the use of standards
- Discuss the value of the Accreditation Scheme for Conformity Assessment (ASCA)

Standards and Conformity Assessment Program (S-CAP)

Consensus Standards: A global regulatory tool

- Crowd-sourced
- Enhance device quality and safety
- Reduce regulatory burden
- Streamline conformity assessment
- Harmonize regulatory practices

Standards and Conformity Assessment Program (S-CAP)



S-CAP goal: advance the development and use of regulatory-ready standards

Standards Recognition Program

'Recognition' - FDA's formal identification of a standard after determining that it is appropriate for manufacturers to declare conformance (with a declaration of conformity) to meet relevant requirements.

The FDA:

- Encourages external and internal stakeholders to nominate standards for recognition
- May recognize all, part or none of the standard
- Will publish the decision rationale
- Regularly updates recognition and non-recognition decisions
  - Recognized Consensus Standards Database
  - Non-recognized Consensus Standards Database
- May withdraw recognized standards, as appropriate

Recognition and Withdrawal of Voluntary Consensus Standards guidance
www.fda.gov/regulatory-information/search-fda-guidance-documents/recognition-and-withdrawal-voluntary-consensus-standards

Standards in Device Regulatory Review

Using FDA-Recognized Standards

FDA strongly encourages the use of recognized standards in premarket submissions

FDA recognition communicates how a standard can address a particular requirement

Declarations of conformity are used with recognized standards, reducing the documentation submitted to FDA

Declaration of Conformity

- Attestation that the device conforms with the cited FDA-recognized standard
- If the manufacturer declares conformity with a recognized standard, a DOC accompanies the submission
- DOCs generally reduce the documentation needed to be included – ***and reviewed*** - in a submission
- Supplemental Documentation is provided based upon the construction of the standard itself.

‘General Use’ of Standards

Choose ‘General Use’ when citing:

- Non-recognized standards
- A recognized standard without submitting a DOC
- A recognized standard where deviations have been made to the methodology

**** For General Use, complete test reports should be submitted - *and will be reviewed* ****

Accreditation Scheme for Conformity Assessment (ASCA)

What is ASCA?

- Accreditation Scheme for Conformity Assessment (ASCA)
- Voluntary program leveraging a well-established international conformity assessment infrastructure
- Capitalizes on voluntary consensus standards in device development and review
- "Puts standards to work" in conformity assessment

← Popular standards

ISO/IEC 17025

Testing and calibration laboratories

ISO/IEC 17011:2017

Conformity assessment — Requirements for accreditation bodies accrediting conformity assessment bodies

ASCA Goal: Streamline conformity assessment in premarket review

- Reduces time needed for conformity assessment element of device review
  - Less need for Additional Information questions, lengthy internal consults and complete test report review
- Removes guesswork about supplemental documentation needs
  - Provides templates for the only documentation needed:
    - ASCA Declaration of Conformity
    - ASCA Summary Test Report
- Improves quality of testing
  - Addresses testing issues for which FDA commonly identifies concerns

ASCA Standards: Biocompatibility

- Majority of medical devices need biocompatibility assessment
- ASCA includes the nine most common biocompatibility test methods
- Nine ASCA Summary Test Report templates are available

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 10993-23*	In Vivo Dermal Irritation, Intracutaneous Reactivity Irritation
ISO 10993-10*	Closed Patch Sensitization
ISO 10993-10* and ASTM F720	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

**ISO 10993-10:2010 split into ISO 10993-10:2021 and ISO 10993-23:2021.*

**ISO 10993-10:2010, ISO 10993-10:2021, and ISO 10993-23:2021 are all included in ASCA.*

ASCA Standards: Basic Safety and Essential Performance

- 90 standards
- Broad utilization across all medical electrical devices
- One ASCA Summary Test Report template

Standard	Standard Title
60601-1	Medical electrical equipment – Part 1: General requirements for basic safety and essential performance (along with the FDA-recognized collateral and particular standards in the IEC/ISO 60601-80601 series)
IEC 61010-1	Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 1: General requirements (along with the FDA-recognized particular standards in the IEC 61010 series)

Example: Infusion Pump with Administration Set

Both ASCA standards families apply:

- Administration set: biocompatibility
- Infusion pump: basic safety and essential performance

Biocompatibility Assessment

Contact type (Tubing)

- Prolonged (>24 hr to 30 days) indirect blood contact

ASCA Biocompatibility Assessment

- MEM Elution Cytotoxicity
- GPMT Sensitization
- Intracutaneous Reactivity Irritation
- Acute Systemic Toxicity
- Material Mediated Pyrogenicity
- Hemolysis (indirect method)

Infusion Pump: Biocompatibility Regular vs ASCA Review

Biocomp testing	Complete Test Report	ASCA Summary Test Report
Review staff	Reviewer may need consult	No need for consult
Number of pages	10-20 pages/method	2-3 pages/method
Review time	Minimum 90 min/method	10-15 min/method
Total review time for six tests	Minimum 10.5 hours	70-90 min total

Example ASCA Summary Test Report: Cytotoxicity

ASCA Test Method: Cytotoxicity – MEM Elution (ISO 10993-5)
Administrative Information

1. Testing Laboratory Name: Test Lab ABC
2. ASCA Testing Laboratory Identification Number: TL-999
3. Testing Location(s): 123 Main St, XXX, Virginia
4. Testing Date(s): February 1st, 2022—February 28, 2022
5. *ASCA Accreditation* Status on the Date(s) of Testing:
   - ☒ Standard (and particular test method) was in testing laboratory's scope of *ASCA Accreditation*
     - ☒ *ASCA Accreditation* was not suspended

ASCA Test Article Prep SOP#: *SOP-SamplePrep-123-Rev2.0, SOP-SampleExtr-456-Rev3.0*

☒ 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[1] (e.g., filtering, extract manipulation, pH adjustment):

Description of deviations/amendments

Test Article:
☒ Entire final finished device
☐ Representative sample selection per SOP
☐ Other:[2] *[DESCRIBE]*

Extraction Solvent:
☒ MEM with 5-10% animal serum
☐ Other:[3] *[DESCRIBE]*

Extraction Ratio:
☒ 6cm²/ml (<0.5mm thick)
☐ 3cm²/ml (0.5-1.0mm thick or molded items > 1.0mm)
☐ 1.25cm²/ml (elastomers > 1.0mm thick)
☐ Other:[4] *[DESCRIBE]*

Extraction Conditions:
☐ 37°C, 24 h
☒ 37°C, 72 h
☐ 50°C, 72 h
☐ 70°C, 24 h
☐ 121°C, 1 h
☐ Other:[5] *[DESCRIBE]*

☒ 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.[5]

ASCA Test Method SOP #: *SOP-ASCA-MEM-789-Rev2.0*

☒ 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:[6]

Description of deviations/amendments

Results:[7]

	48 hr Results	72 hr Results	Conclusion
Vehicle Control	Grade 0/0/0	Grade 0/0/0	Performed as expected
Negative Control HDPE	Grade 0/0/0	Grade 0/0/0	Performed as expected
Positive Control Latex	Grade 4/4/4	Grade 4/4/4	Performed as expected
Test Article Extract (100% neat)	Grade 0/0/0	Grade 0/0/0	Non-cytotoxic

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.

John Standards — 3/15/2022
Name: [TYPED NAME POSITION] — Date

Basic Safety and Essential Performance Testing

- Electrical Equipment Standards
  - IEC 60601-1
  - IEC 60601-1-2
  - IEC 60601-1-12

  * Also others including Usability, Home Use etc….

See FDA guidance "Infusion Pumps Total Product Life Cycle: Guidance for Industry and FDA Staff":
www.fda.gov/regulatory-information/search-fda-guidance-documents/infusion-pumps-total-product-life-cycle

Infusion Pump Model: Electrical Safety and EMC

60601-1, 60601-1-2 and 60601-1-12	Non-ASCA Testing: Complete Test Report	ASCA Testing: ASCA Summary Test Report
Review staff	Reviewer may need consult	No need for consult
Page count	~ 150 pages total	~ 10 pages total
Estimate of review time	~ 10 hours	~ 1.5 hours

ASCA Submission: ASCA versus Non-ASCA Testing

Real-world Class II Device	Non-ASCA Testing (60601-1-2)	ASCA Testing (60601-1)
Deficiencies	1 major 3 minor	0
Length of report	46 pages	9 pages

IEC 60601-1-2 review

- IEC 60601-1-2: complete test reports include images of the test set-up
  - Poor or unclear test set-ups, could raise deficiencies (see example below):

    In your electromagnetic compatibility (EMC) report, you stated that the testing is done on the x, y, and z-axes. However, in your test setup, you have shown the horizontal plane is improperly oriented and has a coil size smaller than the full equipment under test (EUT). This standard is intended to demonstrate common and reproducible basis for evaluating the performance of your device applications when subjected to magnetic fields at power frequency. The processing unit of the device should be exposed during testing. We request that you clarify how the EUT was exposed to x, y, and z axes given the demonstrated test setup. If the processing system was not adequately exposed, we request that you perform new testing demonstrating the device is safe when subjected to magnetic fields at power frequency.

- Using ASCA, we have confidence in ASCA-accredited labs' methods and results
  - No deficiencies would be identified for testing methodology/set-up

ASCA Submissions: Early Experience

- Submissions in-house spanning OHTs 1-7
- ASCA Summary Test Reports used the templates provided in the ASCA guidances
- All critical data and testing conditions captured
- Easier and faster than traditional review

FDA Standards Resources

- **Standards & Conformity Assessment Program**
  www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/standards-and-conformity-assessment-program#intro

- **FDA Recognized Consensus Standards Database**
  www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

- **Non-recognized Standards Database**
  www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/nr_results.cfm

- **Email us at: CDRHStandardsStaff@fda.hhs.gov**

Relevant Guidances

- **Recognition and Withdrawal of Voluntary Consensus Standards guidance**
  www.fda.gov/regulatory-information/search-fda-guidance-documents/recognition-and-withdrawal-voluntary-consensus-standards

- **Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices guidance**
  www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices

- **Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions: Guidance for Industry and Food and Drug Administration Staff**
  www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket

ASCA Resources

- **ASCA web page**

  www.fda.gov/medical-devices/standards-and-conformity-assessment-program/accreditation-scheme-conformity-assessment-asca

- **ASCA program guidance**

  www.fda.gov/regulatory-information/search-fda-guidance-documents/accreditation-scheme-conformity-assessment-asca-pilot-program

- **ASCA Standards-specific guidances**
  - **Basic Safety and Essential Performance standards-specific guidance:** www.fda.gov/regulatory-information/search-fda-guidance-documents/basic-safety-and-essential-performance-medical-electrical-equipment-medical-electrical-systems-and
  - **Biocompatibility standards-specific guidance:** www.fda.gov/regulatory-information/search-fda-guidance-documents/biocompatibility-testing-medical-devices-standards-specific-information-accreditation-scheme

- **Ask ASCA! ASCA@FDA.HHS.GOV**

Knowledge Check

Using standards confers the following advantages (choose all that apply):

a. Stifles international trade

b. Promotes device quality

c. Enhances global harmonization

d. Adds time to the conformity assessment element of device review

Knowledge Check

ASCA stands for:

a. Aggregation of Standards and Confirmation Association

b. Accreditation Scheme for Conformity Assessment

c. Agency for Safety and Confirmation Analysis

d. Additional Standards for Capital Assessment

Summary

- S-CAP advances development and use of regulatory-ready standards
- Consensus standards are an invaluable tool to improve device quality and promote global harmonization
- ASCA testing streamlines device review and enhances quality of testing

Questions