U.S. FOOD & DRUG ADMINISTRATION

Breakout Session I: Biocompatibility (Day 2)

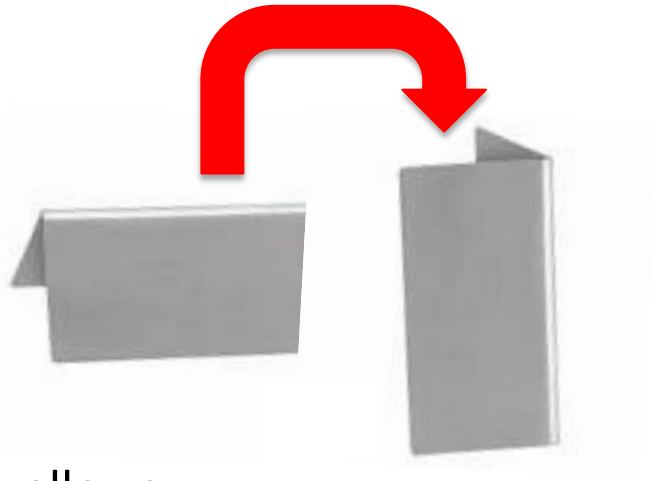
ASCA Public Workshop

May 22-23, 2018

Breakout Session Logistics (D2)

Ground Rules – Day 2 Roundtable:

- Tent cards upright to comment
- State name prior to each comment



Webcast link:

- https://collaboration.fda.gov/ascabreakout/
- Use the "chat" function for comments/questions
- Moderators will share from chat comments as time allows

WiFi Access:

- Username: FDA-Public
- Password: publicaccess

Other:

- Box lunches, snacks and drinks are available for purchase in the lobby
- Visitors can only access Building 31 (workshop site)

Agenda

- Test-Specific Biocompatibility Roundtable Discussion: Challenges, Key Steps, Proficiency
  - Proposed *In Vitro* Biocompatibility Tests for ASCA Pilot
  - Proposed *In Vivo* Biocompatibility Tests for ASCA Pilot
- Biocompatibility Breakout Day 2 Wrap Up

Proposed Biocompatibility Tests for ASCA Pilot

- *In Vitro* Tests:
  - MEM Elution Cytotoxicity (ISO 10993-5)
  - Hemolysis (ISO 10993-4, ASTM F756)
  - Complement Activation (ISO 10993-4)
- *In Vivo* Tests:
  - Guinea Pig Maximization (GPMT) & Closed Patch Sensitization (ISO 10993-10)
  - Intracutaneous Reactivity & Dermal Irritation (ISO 10993-10)
  - Acute Systemic Toxicity (ISO 10993-11)
  - Material-Mediated Pyrogenicity (ISO 10993-11, USP <151>)

Biocompatibility Roundtable Panel Members

- FDA:
  - Molly Ghosh, Expert Toxicologist
  - Jennifer Goode, Biocompatibility Program Advisor
  - Shuliang Li, Senior Standards Advisor
- Testing Labs:
  - Melissa Cadaret, Director, Biocompatibility (NAMSA)
  - Jen Kringstad, Director of InVitro Testing Operations (Wuxi Apptec)
  - Laurence Lister, Director of Biocompatibility Services (Toxikon)
  - Ryan Ross, Associate Department Head, Cell Services (Toxikon)
  - Li Yang, Sr. Scientific Director (Wuxi Apptec)

NOTE: Active audience participation encouraged to better understand input from all attendees.

IN VIVO BIOCOMPATIBILITY TESTS

Guinea Pig Maximization (GPMT) & Closed Patch Sensitization (ISO 10993-10)

- Animal handling (e.g., shaving, wrapping, clinical observations)
- Application of test samples (e.g., GPMT intradermal injections)
- Scoring competency (e.g., ID of positive responses)
- Interpretation of findings (e.g., response frequency/ intensity, re-challenge)

Q1: Are there other critical components for sensitization testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

Intracutaneous Reactivity & Dermal Irritation (ISO 10993-10)

- Animal handling (e.g., shaving, clinical observations)
- Application of test samples
- Scoring competency (e.g., ID of positive responses)
- Irritation Index/Score calculation
- Interpretation of findings

Q1: Are there other critical components for irritation testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

Acute Systemic Toxicity (ISO 10993-11)

- Animal handling
- IP and IV injections
- Clinical observations
- Interpretation of findings

Q1: Are there other critical components for acute systemic toxicity testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

Material-Mediated Pyrogenicity (ISO 10993-11, USP <151>)

- Animal handling and probe placement
- IV injections

Q1: Are there other critical components for material mediated pyrogenicity testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

IN VITRO BIOCOMPATIBILITY TESTS

MEM Elution Cytotoxicity (ISO 10993-5)

- Scoring competency
- Interpretation of findings

  (e.g., Grade 3/1/1: toxic/non-toxic)
- Dose ranging studies: serial dilutions

Q1: Are there other critical components for MEM elution cytotoxicity testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

Hemolysis (ISO 10993-4, ASTM F756)

- Representative sample selection (small quantities)
- Dilutions (multi-step blood/test samples)
- Absorbance standard curve
- Supernatant assessment
- Calculations
- Interpretation of findings

Q1: Are there other critical components for hemolysis testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

Complement Activation (ISO 10993-4)

- Representative sample selection (small quantities)
- Dilutions
- Small volume pipetting techniques
- Anticoagulant use
- Calculations (e.g., graphing, statistical analyses)
- Interpretation of findings

Q1: Are there other critical components for complement activation testing that could impact study results?

Q2: How is technician competency for these issues assessed, including proficiency assessment frequency?

Common Issues: All Tests

Test articles:

- What was tested?
- How were extraction conditions selected?
- Was there degradation of test sample?
- Were there particles/color change/turbidity noted in test extract?

Controls:

- Trending/analysis of control results and related decisions?

BREAKOUT I: BIOCOMPATIBILITY WRAP-UP

Breakout I: Biocompatibility Wrap-up

- D1:
  -
- D2:
  -

Thank You

NEXT SESSION:

- Plenary Session (11:15 am-12:15 pm) in Great Room B/C
  - Summary of Breakouts on the ASCA Scheme to the Standards Outlined in the Pilot.
  - Webcast link:

https://collaboration.fda.gov/ascaplenarybreakout/

FURTHER QUESTIONS?

- Please email: standards@cdrh.fda.gov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