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/](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:
  
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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