Challenges in Non-Clinical Testing of Hemostatic Medical Devices for Trauma Use

Charles N. Durfor, Ph.D.
FDA/CDRH/ODE/DSD
(301) 796-6970
Various Compositions of Hemostatic Devices

- Animal Tissue (e.g., Collagen, Gelatin, Chitosan, Thrombin)
- Derived from Plants (e.g., Alginate)
- Mineral-Based (e.g., Kaolin, Zeolite)
- Synthetics (e.g., Polyester, Carboxymethylcellulose)
Issues with Animal Source Material

- Sourcing Issues
  - Animal Husbandry
  - Control of Tissue Collection
  - Manufacturing Controls for Animal Tissue Components
  - Sterilization (and Virus Validation Studies)

Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices) (Draft)
http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm381379.htm
Considerations for Non-Clinical Testing

For Potential Battlefield Products

– Consider Environmental Conditions
  . Temperature
  . Altitude
  . Humidity
  . Robustness of Packaging

– Consider the User
  . Labeling revisions based on bench/animal experience

- Series of standardized tests
- Dependent on:
  - Time of contact
  - Type of contact
- Works for many, but not all biomaterials

*Points of Interest* (pp. 9 – 13)

- Final Product or Representative Sample?
- *In Situ* Polymerizing Material
- Bioabsorbable Material
- Biological Response Resulting from Device Mechanical Failure
- Submicron or Nanotechnology Components
- Multiple components or materials in a single sample

- Sources of Information
  - In-house studies
  - Master Files from Raw Material Suppliers
  - Published Literature
  - Others? (e.g., MSDS)
Situations where Standard Biocompatibility Tests may be less than optimal

• **Final Product or Representative Sample?**
  - Animal Tissue / Scaffold construct
  - Sealant / Patch – Crosslinked *in situ*
  - Surgical Instrument Models for TSE

  “Certain instrument features are particularly difficult to clean – hinges, mated surfaces and lumens. Many TSE investigators are now using small (5 mm) stainless steel wires coated with inoculum in their studies of TSE transmissibility. The material is a suitable stand-in for many instruments.”  

(page 7 – FDA Briefing Material 9/27/05 – Panel Mtg.)
Situations where Standard Biocompatibility Tests may be less than optimal

- *In Situ* Polymerizing and Bioabsorbable Materials
  - Consider the Reagents
  - Consider the Reaction
  - Consider the Final Product
  - Consider the Decomposition Products
  - Kinetics of Resorption
Situations where Standard Biocompatibility Tests may be less than optimal

Submicron or Nanotechnology Components

- Unique properties of submicron / nanotechnology components, (e.g., large surface area / particle, aggregation, agglomeration, immunogenicity, toxicity (altered release kinetics?)

- Rationally designed features that modify host cell response.
Situations where Standard Biocompatibility Tests may be less than optimal

Submicron or Nanotechnology Components

Consider:

– Careful characterization of the test sample and extract conditions (e.g., solvent type) to avoid non-clinically relevant testing artifacts

– Assure that the test article is representative of the clinical product
Resources

Device Search Engines
PMA/510k/MAUDE
http://www.fda.gov/cdrh/databases.html

CDRH - Guidance Database Search Engine
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm


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