Standards Use Supporting Regulatory Applications to FDA for Cell & Gene Therapy Products

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Scope of Presentation

• Introduction
  – Definitions
  – FDA Policy

• **Current Standards Activities** in the Office of Cellular, Tissue and Gene Therapies (OCTGT) with examples

• Recent government standards workshop

• Summary
Regulations vs. Standards

- **Regulations**
  - Government implementation of statues that have the force of law
  - Define specific requirements for safety
  - Provide accurate information to health professionals and consumers

- **Standards**
  - Voluntary
  - Frequently developed outside of the government
  - Written standards describe how manufacturers might meet regulatory requirements
  - Physical standards provide accepted “benchmark” materials
Types of Standards

- Performance characteristics
- Testing methodology
- Manufacturing practices
- Scientific protocols
- Compliance criteria
- Ingredient specifications
How do standards support the regulatory process?

- Help a sponsor meet regulatory requirements
- Facilitate product design
- Improve time to market
- Leverage industry efforts
- May lead to international harmonization
FDA Regulations & Policy for Standards Use & Development

- FDA’s Staff Manual Guide SMG 9100.1
  - Agency-wide policy, FDA will use harmonized standards in lieu of gov’t unique standards except when they conflict with regulations.

- 21 CFR 10.95 (a)
  - Describes FDA participation in outside standards setting activities

- Food, Drug and Cosmetic Act 514(c)
  - Describes standards recognition program in CDRH and use of standards for medical devices
Standards Use for Cell & Gene Therapy Products

- Sponsor can cite a written standard in their regulatory application
- Sponsor can use a reference material in the development and testing of their product.
Referencing Written Standards in a Regulatory Application to CBER

- A standard can be used in whole or part.
- Sponsors should submit a complete reference to the standard including version to CBER/OCTGT to ensure the standard is appropriate for the intended purpose.
- Once a specific version of a standard is considered acceptable following review, implementation of a new version of the standard should be discussed with OCTGT to determine continued acceptability.
Current Standards Activities for Cell & Gene Therapy Products
ISO Technical Committee 276 Biotechnology

Working Groups

1. Terminology
2. Biobanks and Bioresources (for research)
3. Analytical Methods
4. Bioprocessing
ISO Tissue Engineering Technical Sub-Committees

- **TC150/SC7 Implants for Surgery, Tissue Engineered Medical Products**
  - WG 1 Management of Risk
  - WG 2 General Guideline of Safety Test
  - WG 3 Tissue-Engineered Medicinal Products for Skeletal Tissues

- **TC194/SC1 Biological Evaluation of Medical Devices, Tissue Products Safety**
  - WG 1 Risk assessment, terminology and global aspects
  - WG 2 Sourcing controls, collection and handling
  - WG 3 Elimination and/or inactivation of viruses and TSE agents
  - WG 4 TSE Elimination
Examples of ISO Standards Applicable to Cell Therapy Products

- ISO 10993-XX multiple standards (e.g. chemical characterization of materials, guidance on tests to evaluate genotoxicity, etc.
- ISO/TR 373137:2014 *Cardiovascular biological evaluation of medical devices-Guidance for absorbable implants*
- ISO/TR 16379:2014 *TEMPS- Evaluation of anisotropic structure of articular cartilage using diffusion tensor MRI*
- ISO 13022:2012 *Application of Risk Management to Viable Materials of Human Origin Used for the Production of Medical Products*
American Society for Testing Materials International ASTM

Committee F04: Medical and Surgical Devices

Subcommittees for TEMPS

F04.41 Classification and Terminology
F04.42 Biomaterials and Biomolecules
F04.43 Cells and Tissue Engineered Constructs
F04.44 Assessment – preclinical evaluation of TEMPs
F04.45 Adventitious Agent Testing
F04.46 Cell Signaling
Examples of ASTM Standards for Cell Therapy Products

- **F3106-14** Standard Guide for in vitro Osteoblast Differentiation Assays

- **F2998-14** Guide for Using Fluorescence Microscopy to Quantify the Spread Area of Fixed Cells

- **F2944-12** Standard Test Method for Automated Colony Forming Unit (CFU) Assays—Image Acquisition and Analysis Method for Enumerating and Characterizing Cells and Colonies in Culture

- **F2315-11** Standard Guide for Immobilization or Encapsulation of Living Cells or Tissues in Alginate Gels
ATCC SDO Standards

- **Written Standard:**
  - ASN-0002- Authentication of Human Cell Lines: Standardization of STR Profiling

- **Reference Materials/Physical Standards**
  - ATCC VR-1516 Adenovirus Type 5
  - ATCC VR-1616 Adeno associated virus Type 8
Harmonization Standards

- World Health Organization (WHO)
  - WHO Requirements, Recommendations and Guidelines
  - Physical Standards for manufacture and control of biological products

- International Conference on Harmonisation (ICH)
  - No standards for cell therapy at this time.
  - Considerations documents for gene therapy
Recent Government Workshops on Standards

- Synergizing Efforts in Standards Development for Cellular Therapies and Regenerative Medicine Products (March 15, 2014) sponsored by FDA/CBER/OCTGT
  - Goal: bring together a broad range of FDA stakeholders interested in the clinical development of cellular therapies and regenerative medicine products to inform on the roles of FDA and other federal agencies in standards development, the different types of standards, and organizations that are currently developing standards for these products.
Factors Important for Standards Development in the Cell Therapy/Regenerative Medicine Space

• Awareness of existing standards- (e.g., mechanism to identify existing standards, a mechanism to allow widespread commenting on draft standards under development by various Standards Development Organizations (SDOs)

• A mechanism to identify the need for specific standards
Factors Important for Standards Development in the Cell Therapy/Regenerative Medicine Space (continued)

- Education on standards development and standards use at scientific conferences, society meetings and universities
- Coordination between groups interested in standards development to prevent duplication of efforts
- Funding support and scientific interest in developing the needed standards
Recent Government Workshops on Standards (continued)

• Strategies to Achieve Measurement Assurance for Cell Therapy Products (May 11-12, 2015), sponsored by NIST
  – Goal: Examine approaches for improving confidence in the measurements that are necessary for bringing cell therapy products to market.
Summary

• Written standards complement regulations by describing how manufacturers might meet the regulatory requirements for a particular product.
• Standards can complement FDA guidances by providing an alternate approach or an acceptable technology.
• Standards address numerous topics such as design, manufacturing, professional practices, nomenclature, and testing.
• Standards can be useful tools throughout the life cycle of a product in many disciplines.
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http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm
Public Access to CBER

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