Standards Coordinating Body
For Cellular/Gene and Regenerative Therapies and Cell-Based Drug Discovery

Cell Therapy Liaison Meeting
Bethesda, MD
October 19, 2016
SCB Will Significantly Support Existing SDO Efforts

**SCB contributions**
- **Identify and convene experts to prioritize** and provide expertise/knowledge to measurement and standards needs for cellular/gene and regenerative therapies and cell-based drug discovery
- **Perform gap analysis** to identify emerging needs for standards
- **Recommend** projects to address gaps
- **Organize** SCB, NIST and other Agency **workshops** to discuss standards priorities and technical challenges (logistics/financial)
- **Create** and maintain **comprehensive** standards information **resource**
- **Develop web content** with information on standards, services, and products
- **Will participate with NIST and FDA in ISO/TC276 US TAG and ASTM F04**
Recent Survey of Stakeholders that Participate in SDOs/SSOs

Table 11. Interaction with Standards Organizations in the Development of TE/RM Technologies

<table>
<thead>
<tr>
<th>Standards organization</th>
<th>Percent working with them</th>
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<tbody>
<tr>
<td>ASTM</td>
<td>6</td>
</tr>
<tr>
<td>ISO</td>
<td>6</td>
</tr>
<tr>
<td>USP</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
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SCB-NIST MOU and Public-Private Partnership Model

**Collaborative Activities:**

- Identifying and convening of technical experts for standards development
- Identifying **areas of mutual interest** for R&D
- Providing **educational tools** for standard development and use
- **Jointly** planning conferences and **workshops**
- **Disseminating information** regarding existing standards
- Developing web content

**SCB Members & ECC**

**SCB-Internal Process**

**Information Sharing**

**Research Collaborations e.g. CRADA**
“Synergizing Efforts in Standards Development for Cellular Therapies and Regenerative Medicine Products” (FDA Workshop)

Potential collaborative framework

SCB will support SDOs upstream and downstream, and provide expertise and industry consensus within the existing SDO processes, including ISO and ASTM, where FDA is participating, given the importance of the consensus process to standards with the potential for utility in the regulatory review process.

SCB has MOU with NIST as the primary PPP Federal Agency partner; SCB is open to discussing contractual and non-contractual relationships directly with FDA.

SCB requested a call for FDA participation, which can be mediated via an official FDA point-of-contact. Participation in addition to SDO could include workshop participation and involvement in interlab studies.

SCB will provide the draft work plan to FDA prior to launch; discuss high-level aspects of CT sector at CTLM; potential for discussion at MATES again.
Work Plan: Key Activities

Chair: Michael Mendicino, Hybrid Concepts Intl
Co-Chair: Krish Roy, Cell Manufacturing Consortium

Most recent activities:
• WG calls commenced; stakeholder membership has grown significantly
• Established Budget WG liaison
• Established 4 sectors (cell therapy, gene therapy, tissue engineering, drug-discovery); each have had focused priorities discussions per sector

Next Steps:
• Establish official SCB work plan by a team of all stakeholders across all product areas, with both international and Federal Agency representation
• Will align project budget with Budget Working Group
• Determine how best to disseminate work plan to stakeholders and disseminate/gather participant organizations/individuals
• Work with Federal Liaison team on logistics of NIST, FDA and other Agency interactions/activities with regards to work plan, SDO, and SSO activities
• Designated 1-2 project champions for each topic from the work plan WG to develop details with input from the work plan WG
Updates by Sector – Cell Therapy

**Co-leads:** ISCT, ISSCR, CCRM/UHN (Canada), NCMC

**Additional organizations that had input on rankings:** FACT, AABB, ASGCT, Cell & Gene Therapy Catapult (UK), NIBSC (UK), A-STAR (SG), JnJ, MilliporeSigma, ThermoFisher, RoosterBio

**Buckets of activities from rankings:**

- Support/accelerate existing SDO efforts
  - ISO, ASTMi
- Support/accelerate existing SSO efforts
  - e.g., USP
- Outreach via website and workshop content
  - SCB cell therapy website content
  - General and project-specific workshops, SCB-lead or co-sponsored
- Initiate novel SCB projects
Most Highly Ranked Ongoing SDO and SSO Activities

ISO (SDO): Cell Characterization (ISO TC276 WG3)
Characterization of Cells
• SCB can help solicit/collection critical stakeholder input for strategic planning of this project; potentially provide pre-standards resources (e.g., interlab data, analyses)
• Project champion to be SCB ISO expert(s)

ASTMi (SDO): (TBD once TE sector and CT sector communicate on ongoing activities)
• SCB can help solicit/collection critical stakeholder input for strategic planning of this project; potentially provide pre-standards resources (e.g., interlab data, analyses)
• Project champion to be SCB ASTMi expert(s)

USP (SSO): Rapid Microbiological Methods (RMM)
• Review what has been done and what still needs to be done in coordination with USP; develop SCB project plan contribution
• Need to define project champion – SCB USP representative?
Cell Therapy Sector – ISO and ASTMi

ISO (SDO): Cell Characterization (ISO TC276 WG3)
Characterization of Cells.
- Design of Analytical Methods
- Cell Measurement Process
- Inventory/example of common methods
- Analytical Methods for MSCs

ASTMi (SDO): (1-2 projects from below list TBD once TE sector and CT sector communicate on ongoing activities)

- MSC Discussion. Initially, develop a protocol that would allow the same MSC cells to be transferred to different laboratories and to determine the extent to which they behave in the same manner in the different labs. This protocol could lead to one or more ASTM standard test method(s).
- New SG for autologous platelet-Rich plasma for use in tissue engineering and cell therapy.
- Test Method for Automated Colony Forming Unit (CFU) Assays – Image Acquisition & Analysis Method for Enumerating & Characterizing Cells & Colonies in Culture
- SG to describe molecular attributes useful to monitor in vitro differentiation multipotent stem cells toward skeletal myocytes.
- SG assessing medical device cytocompatibility with delivered cellular therapies.
Rapid Microbiological Methods (RMM)

• “This guidance addresses considerations for method validation and determining equivalence of an RMM to sterility assays described in 21 CFR 610.12. This guidance, when finalized, will address relevant issues and facilitate the implementation of an RMM for sterility testing.” 21 CFR 610.12 is similar to USP <71>.
• “Rapid microbiological methods are methods designed to provide performance equivalent to the sterility testing methods described in 21 CFR 610.12, while providing results in significantly less time.”

USP Update:

An expert panel was formed last year and is working with the USP Microbiology Expert Committee on the selection and assessment of suitable technologies for the rapid sterility testing of short-life injectable products. Critical user requirement specifications for candidates’ rapid sterility tests were specificity, limit of detection, time to result, improved patient safety, sample preparation, and minimum number of articles tested and quantity per container tested. Several well established candidate technologies will be evaluated for proof of concept studies.
Cell Therapy Sector – Outreach to Define Projects

SCB website
• Not only work with other SCB sectors but leverage existing content externally
  - topic “Population of Cell Therapy Website Content” is a bit duplicative of the work done by and posted on http://www.ahcta.org
  - http://rapidmicromethods.com
  - This and other cell therapy content can be consolidated by SCB staff and cell therapy sector membership to provide a comprehensive and well-advertised resource

SCB workshop(s) to help define novel SCB projects
• Not only “launch” workshop but need topic-specific workshops to review what has been done and where the gaps exist; SCB-led or co-sponsored; output could include publication
  - Flow Cytometry and FACS/MACS isolation standards, research and/or clinical applications
  - Particulates, both safety i.e., what can be potentially harmful, or efficacy e.g., exosomes)
    - Existing ISO and USP guidelines are not directly applicable to cell therapy
    - USP considering revising existing chapter <1046> Cell and Tissue-based products, to include information on the type of technologies used for the measurement of particulates in cell therapy products.
    - Classically a safety concern, but cell themselves are a particulate; so are exosomes!
Cell Therapy Sector – Particulates

• **General Biological Product Standards (21 CFR 610)**
  – “Products shall be free of extraneous material except that which is unavoidable in the manufacturing process described in the approved biologics license application”

• **USP <790> and <1790>**
  – 100% inspection during manufacturing
  – Statistical sampling for final product appearance test (post-thaw)
  – No magnification, adequate light
  – Spec: “Essentially free from visible particulates”

• **ISCT Process and Product Development Subcommittee**
  – Two position publications, “Managing Particulates in Cell Therapy”

• **Blood products vs. Cell therapies?? Examples: Licensed Package Inserts**
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<th>Sectors</th>
<th>Examples of Current Stakeholder* Activities</th>
<th>Stakeholder* Defined Priorities by Sector</th>
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| **Gene and Gene Modified Cell Therapy**     | • Development, characterization, and production of AAV-2 and AAV-8 reference standards  
• Development of lentiviral reference standards                                                                 | • Further characterization of existing AAV ref standards (different serotypes, mammalian vs. bacterial platforms, in vivo testing)  
• Lentivirus reference standards for copy number determination in modified cells, vector purity  
• Standardized methods for AAV vector copy quantification, cell lines/method for infectivity assessment, empty particle ratio  
• Cell counting (total and viable) for HSC, and ID for CD34+                                                                 |
| **Cell Therapy**                            | • ISO TC276 work items such as cell counting  
• NIST measurement assurance for cell therapy activities  
• Other SDO and SSO activities                                                                 | • Support current SDO and SSO activities, such as cell characterization pre-standards work and standards and Rapid Microbiological Methods pre-standards work and standards  
• Develop cell therapy sector landscape and future projects for standards via consolidation/maintenance of resources and outreach                                                                 |
| **Cell-Based Drug Discovery**               | • Publication of stakeholder “call to action” for standards harmonization in market  
• Align standards priorities and technical challenge with efforts of ICH-s7 a/b, CiPA, HESI, ILSI- FDA WG, CSRC                                                                 | • Harmonization of ongoing standards efforts through characterization of cells, recommendations on usage, and further development / iteration of cell types  
• Market and regulatory alignment for manufacturing process consistency, product quality, material management, personal training, equipment and facility parameters  
• Needed expertise for technical documentation of SDO activities                                                                 |
| **Tissue Engineering and Biomaterials**     | • Alignment with ASTM for current standards activities and documentation initiatives (including US Mirror Committee for ISO/TC194)  
• Prioritization of potential near-term projects e.g. organ-on-chip, sterilization, etc.                                                                 | • Assess best practices with ASTM for prioritizing joint SCB projects  
• Review and prioritize with ASTM current and burgeoning standards efforts in TE  
• Potential areas to include: organ-on-chip as a potential QA system to phenotype regenmed cell products in complex microenvironments                                                                 |

* Stakeholders: FDA, ex-US regulators, NIST, ex-US governmental standards entities; gene therapy companies, interested large pharma, gene therapy research institutions, gene therapy societies, gene therapy CxOs, SDO/SSOs *
### Proposed Major for SCB Near-Term Milestones

**Official Launch planned by end of 2016**

- **2Q16**
  - Establish/select charter members to define objectives and select organizational structure
  - Create Steering Committee and Form Working Groups to Guide Launch
  - File for approval of 501c3 tax-exempt status for SCB to operate as foundation
  - Secure Congressional and Administration endorsement

- **3Q16**
  - Develop MOU/CRADA or other framework to engage federal entity – NIST, and launch official PPP
  - Define / finalize short-term project plans

- **4Q16**
  - Establish initial operating budget to include private sector contributions and public grant funding
  - Define long-term funding model to sustain / grow operations
  - Define long-term work plan

- **1Q17**
  - Identify / hire leadership and staff to manage SCB
  - Establish formal strategic plan

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**Progressive international participation**

- Executed / In-Progress
- Planned
• Present SCB work plan topics to FDA and request feedback

• SCB is aware that FDA participates in both ISO and ASTMi standards activities and looks forward to mutual participation on specific projects via the SDO process

• SCB plans to consolidate input on any draft FDA Guidance for Standards released impacting our fields

• SCB thanks FDA for hosting the MATES meeting and looks forward to working with the FDA point-of-contact once determined
Thanks to all Stakeholders that Have Helped Progress the SCB Towards Official Launch!!!