Regulatory Updates for Human Cell Therapy Products:

An FDA Perspective

CASSS Cell and Gene Therapy Products Symposium

Regulatory Updates from Across the Globe

June 12, 2019

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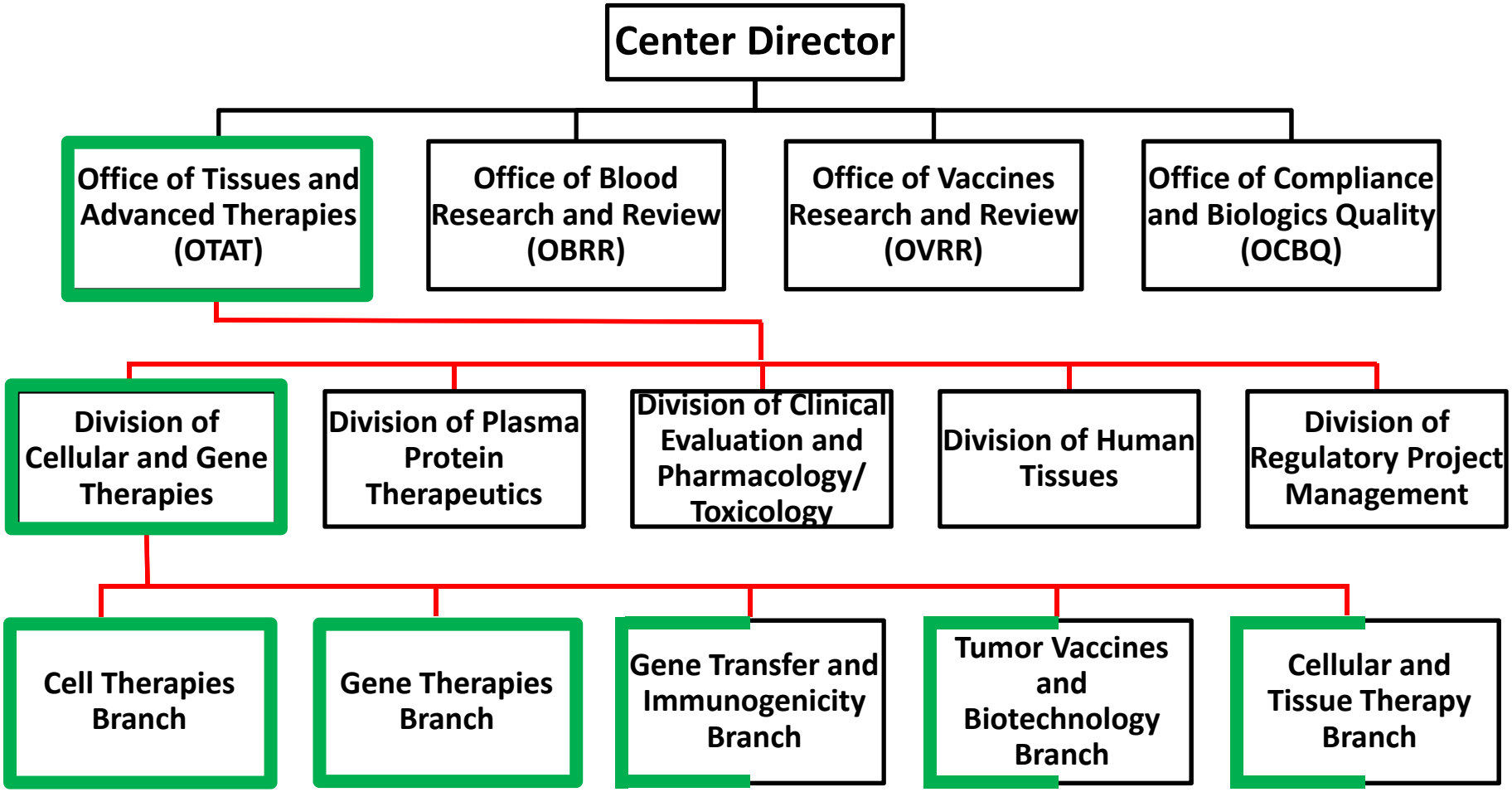
United States Food and Drug Administration

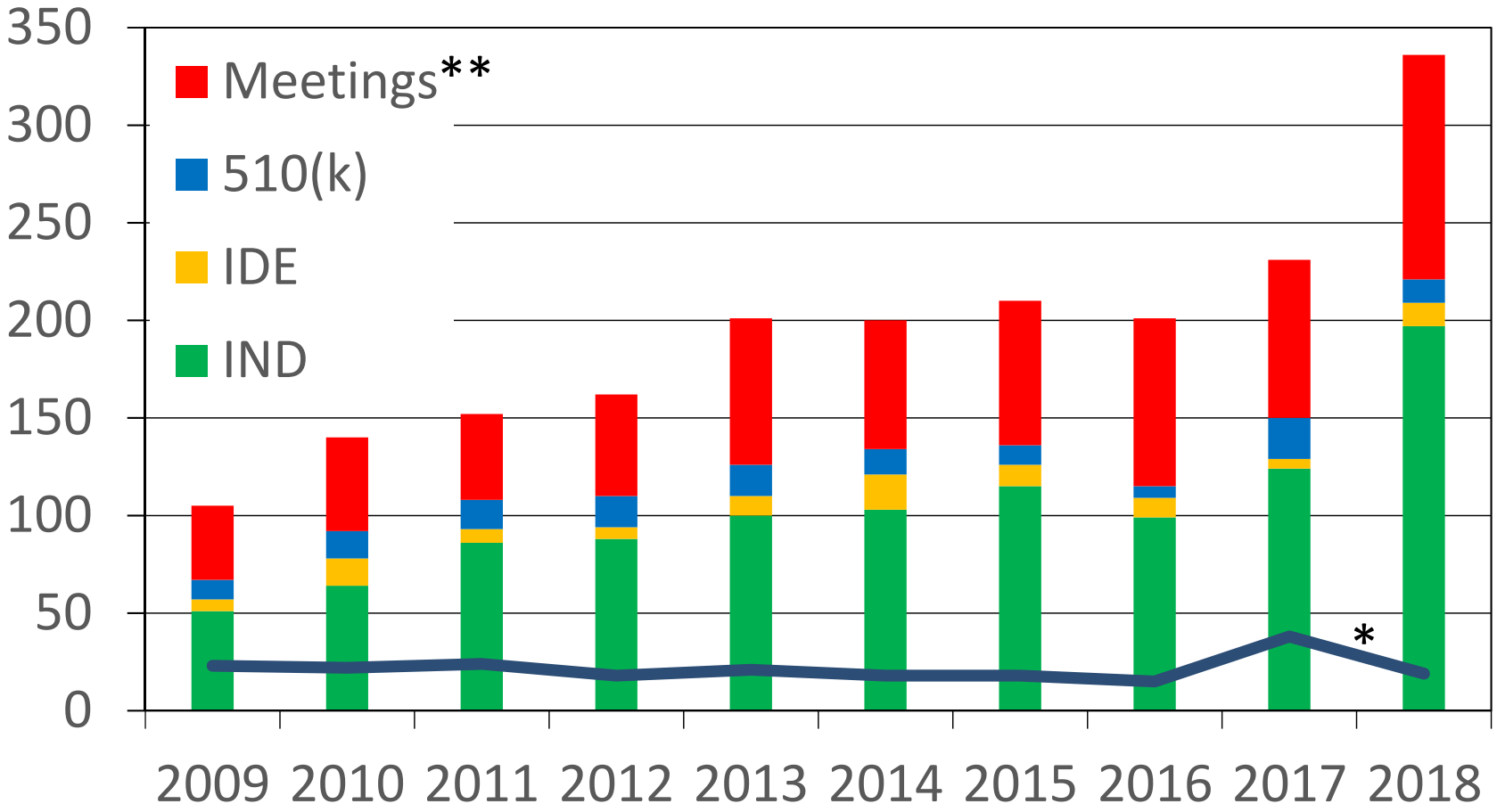
CBER Organization for Pre- and Post-Market Regulation



Human Cell Therapy Products

- **Stem cell and stem cell-derived products**
  - Hematopoietic, mesenchymal, cord blood, embryonic, iPSCs
- **Somatic cell therapies**
  - Pancreatic islets, chondrocytes, keratinocytes, hepatocytes
- **Cancer vaccines and cellular immunotherapies**
  - Cancer cell-based therapies, immune system cell-based therapies
- **Tissue-based therapeutic products**
  - Amniotic membrane, umbilical cord, thymus, amniotic fluid
- **Xenotransplantation products**
- **Combination products**
  - Cells + scaffolds, cell encapsulation for implantation
- **Devices**
  - Processing cells/tissues, delivery of cells/gene therapies

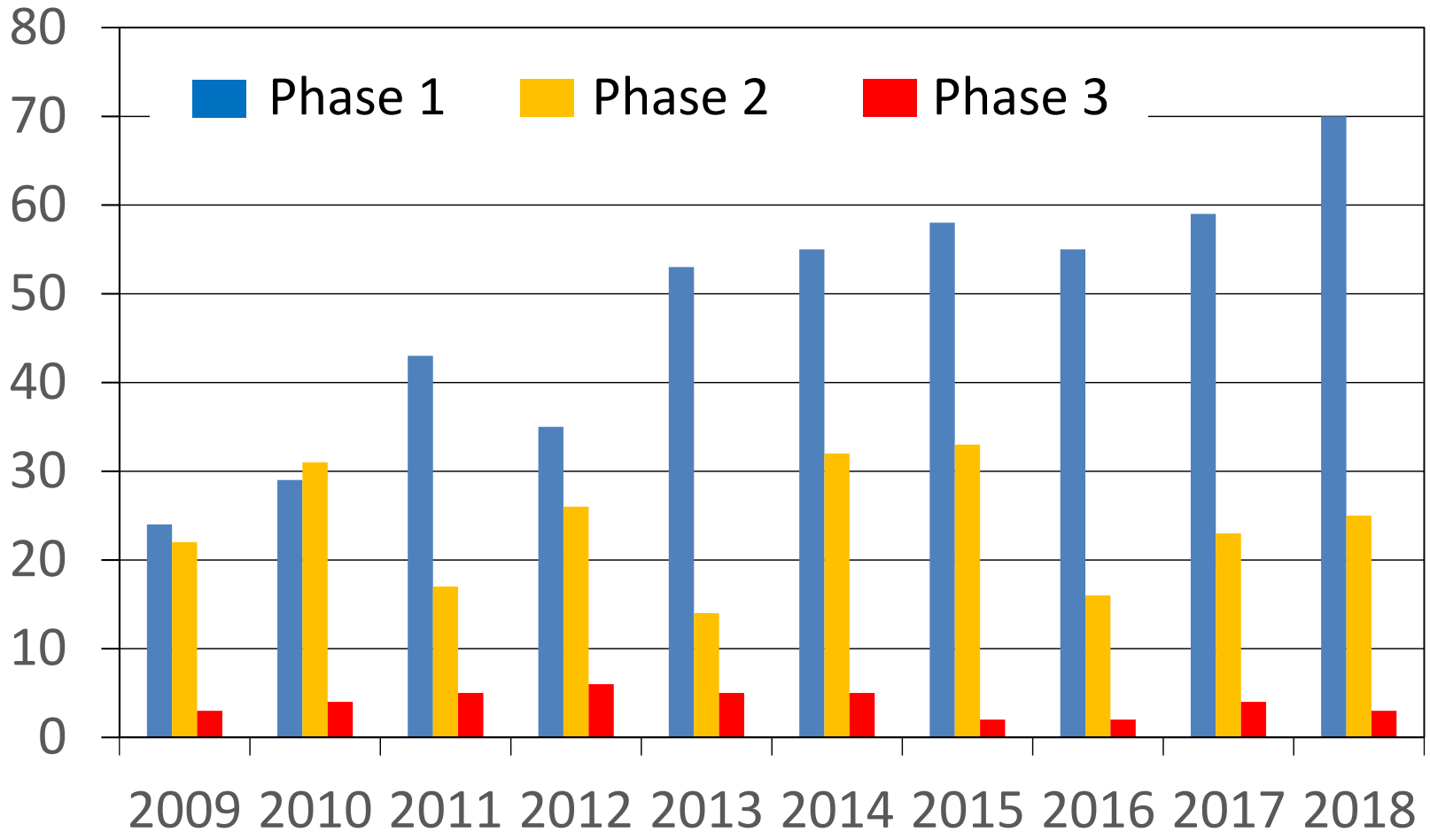
New Cell Therapy Files Received per Calendar Year in OTAT (by Submission Type)



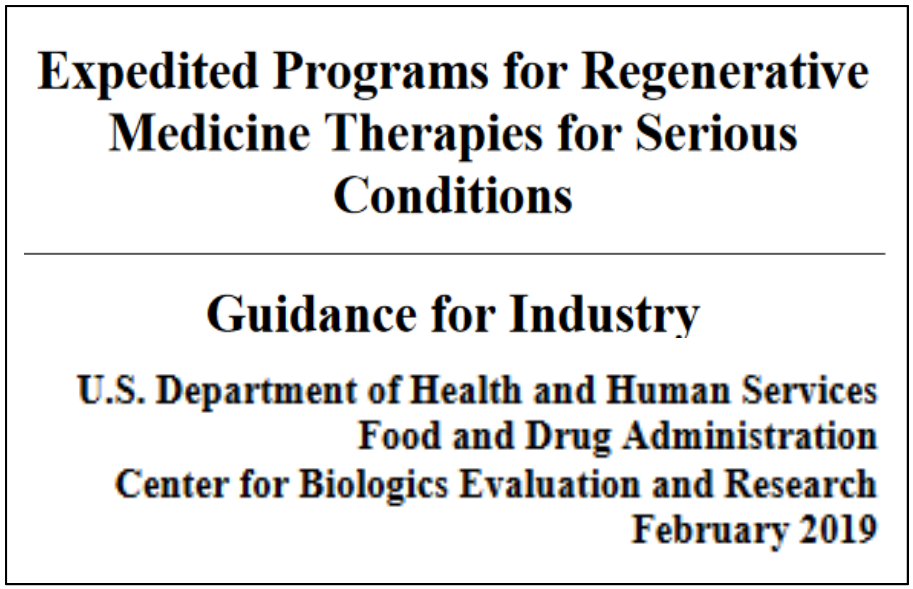
* **Combination products in IND**

** Pre-pre-INDs/INTERACT, Pre-INDs, INDs, Pre-submissions

New Cell Therapy INDs Received per Calendar Year in OTAT (by Clinical Study Phase)

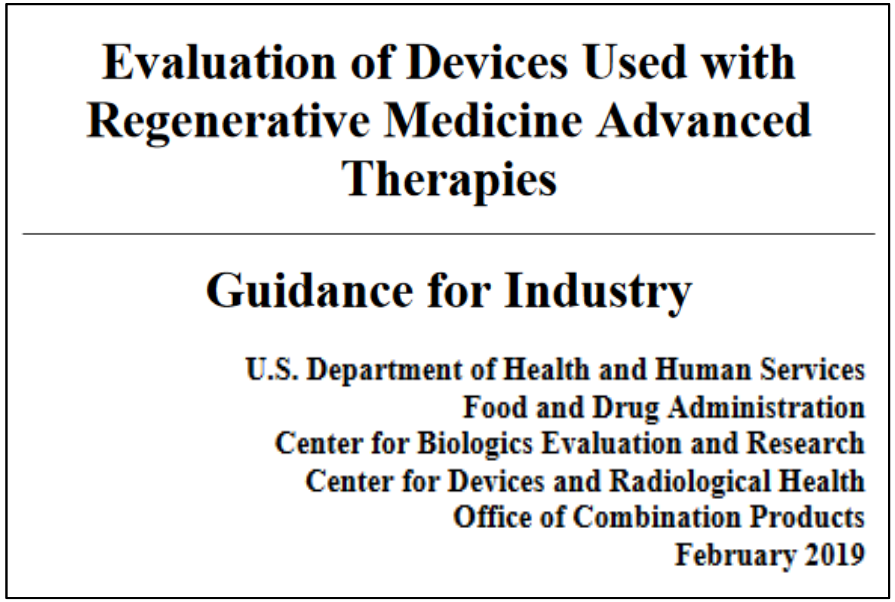


Guidance Document Updates (1)



- Regenerative Medicine Therapies
  - Cell therapies
  - Therapeutic tissue engineering products
  - Human cell and tissue products
  - Human gene therapies
  - Xenogeneic cell products
  - Combination products
- Fast Track Designation
- Breakthrough Therapy Designation
- Regenerative Medicine Advanced Therapy Designation
- Priority Review Designation
- Accelerated Approval
- https://www.fda.gov/media/120267/download

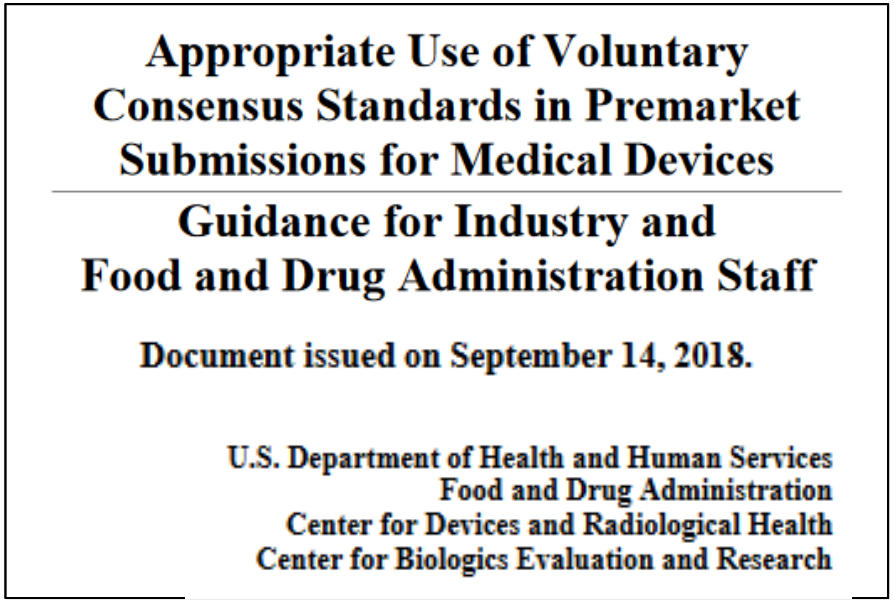
Guidance Document Updates (2)



Evaluation of Devices Used with Regenerative Medicine Advanced Therapies

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
Center for Devices and Radiological Health
Office of Combination Products
February 2019



Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices

Guidance for Industry and Food and Drug Administration Staff

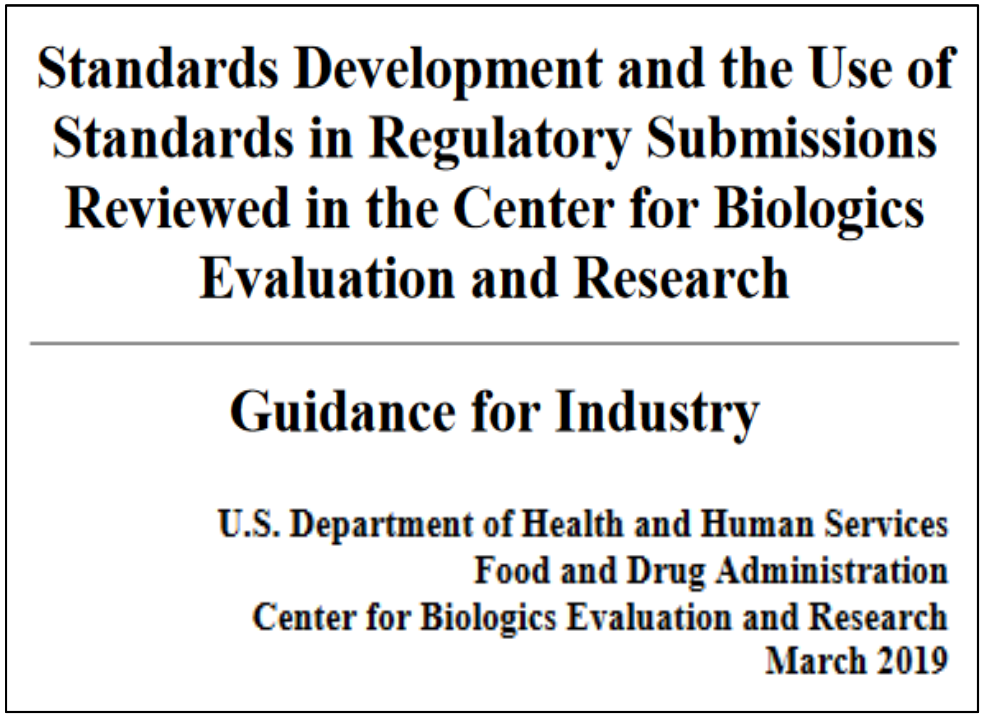
Document issued on September 14, 2018.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- Devices used to:
  - **Recover** - obtain cell/tissue from human donor
  - **Isolate** - process cell/tissue
  - **Deliver** - administer RMAT
- Device Premarket Pathways
- Combination Products
- https://www.fda.gov/media/120266/download

- Appropriate use of FDA recognized and non-recognized consensus standards
- Center for Devices and Radiological Health recognized standards can be used to support CBER-regulated devices
- CDRH-recognized standards available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
- https://www.fda.gov/media/71983/download

CBER's Standards Guidance



- Overview of standards
- How are voluntary standards developed?
- What are the benefits of using voluntary standards?
- What is CBER's policy on accepting standards used in regulatory submissions?

https://www.fda.gov/media/124694/download

Standards Activities at OTAT

- Staff (OTAT researchers, reviewers, and policy makers) act as liaisons to Standards Development Organization (SDO) technical committees to:
  - Facilitate the development of standards that are not in conflict with FDA regulations and policies
  - Increase the likelihood that standards developed will be suitable for regulatory submissions reviewed by FDA
- Work with relevant national and international regulatory agencies to identify and fill gaps

Standards Activities – Update (1)

- 21st Century Cures Act
- Prepared for FDA/CBER
- Provides summary of existing Cell Therapy (73), Gene Therapy (50), Tissue Engineering (67), and Supportive (75) standards
- Concluded: “a critical need for more regenerative medicine standards”

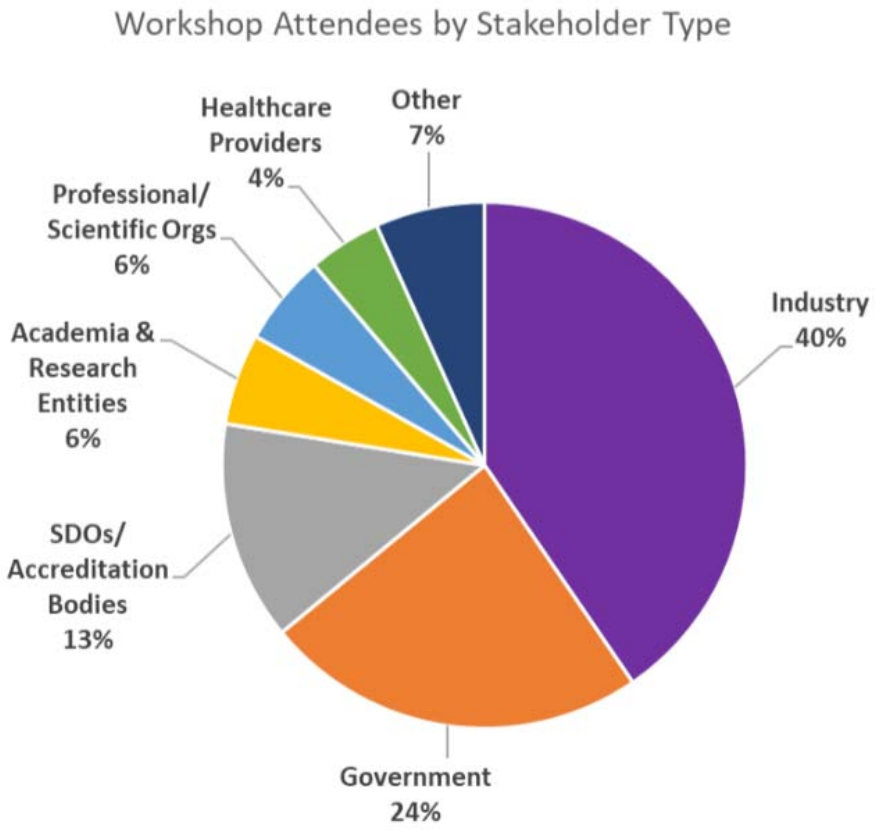
Existing Regenerative Medicine Therapies Consensus Standards Examples

- ASTM F2312-11: Standard Terminology Relating to Tissue Engineered Medical Products
- ASTM F2383-11: Standard Guide for Assessment of Adventitious Agents in Tissue Engineered Medical Products
- ASTM F2315 Standard Guide for Immobilization or Encapsulation of Living Cells or Tissue in Alginate Gels
- ISO 13022:2012: Medical products containing viable human cells - Application of risk management & requirements for processing practices
- ISO 20387:2018: Biotechnology - Biobanking - General requirements for biobanking
- ISO 10993: Biocompatibility

Standards Activities – Update (2)

March 18 - 19, 2019

- Standards development process, participation, and role in improving product quality and safety
- **Identified high-priority standards needs:** cell viability, chain of identity and chain of custody, characterization of scaffold materials, and viral vector gene quantification
- **Focus on**: Characterization of Human Cells for Therapeutic Use and Rapid Microbial Testing Methods



CBER Contact Information

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- **Regulatory Questions:**
  Contact the Regulatory Management Staff in OTAT at OTATRPMS@fda.hhs.gov or Lori.Tull@fda.hhs.gov
- **OTAT Learn Webinar Series:**
  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm
- **References for the regulatory process for OTAT:**
  http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/OtherRecommendationsforManufacturers/ucm094338.htm
- **CBER website:** http://www.fda.gov/BiologicsBloodVaccines/default.htm
- **Phone:** 1-800-835-4709
- **Consumer Affairs Branch Email:** ocod@fda.hhs.gov
- **Manufacturers Assistance and Technical Training Branch Email:** industry.biologics@fda.gov
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