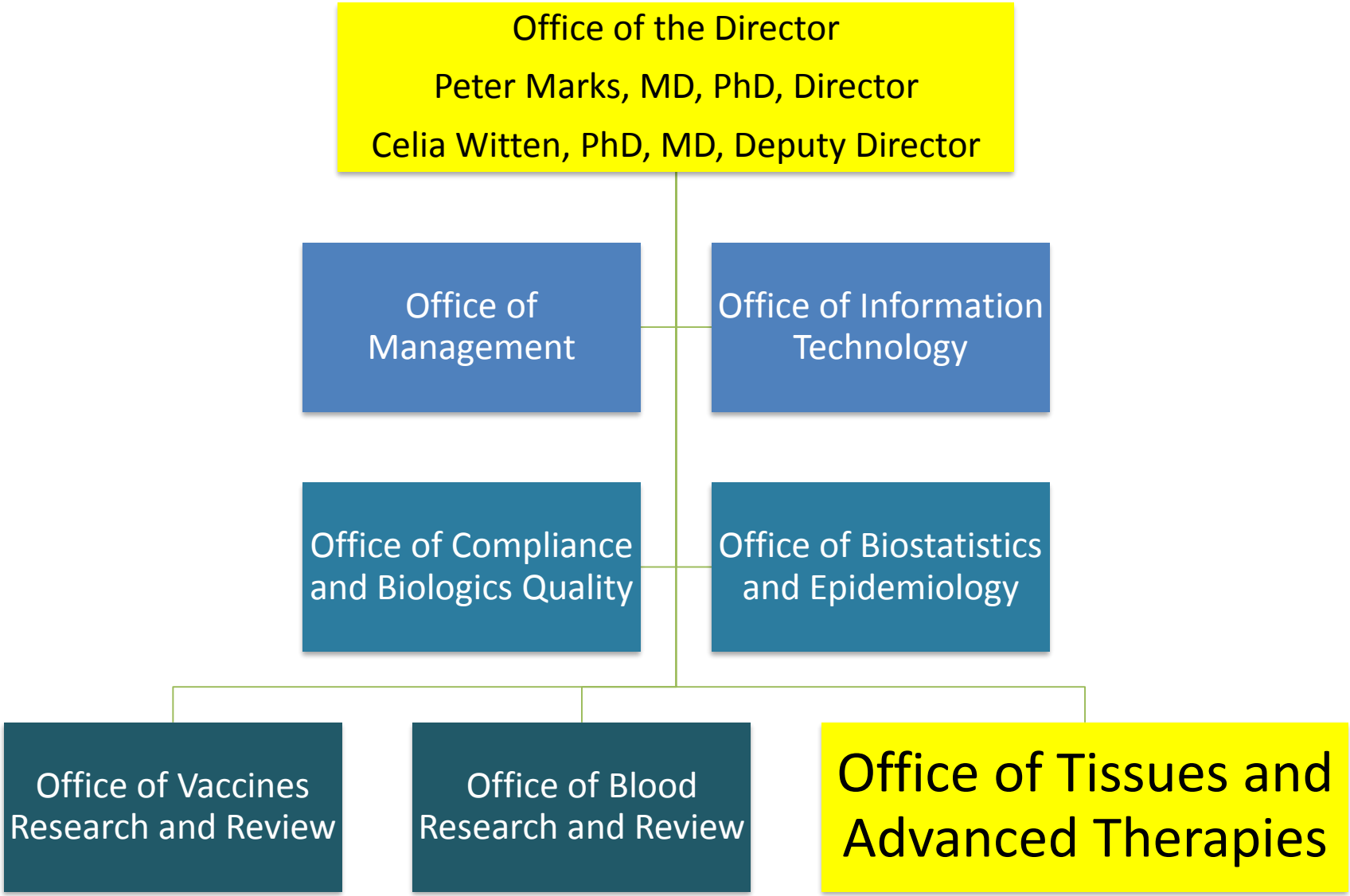
Center for Biologics Evaluation and Research (CBER)



December 13, 2016

21st Century Cures Act: Title III, Sections 3033-3036

- Regenerative medicine provisions:
  - Section 3033: Creates program for designation of regenerative medicine advanced therapies
  - Section 3034: Mandates that FDA develop guidance regarding devices used in the recovery, isolation, or delivery of regenerative advanced therapies
  - Section 3035: Mandates that FDA report yearly to Congress on regenerative advanced therapies
  - Section 3036: Directs Department of Health and Human Services (HHS), in consultation with the National Institute of Standards and Technology (NIST) and stakeholders, to facilitate efforts around development of standards for regenerative medicine therapies and regenerative advanced therapies

21st Century Cures Act
Section 3033: Definition of Regenerative Medicine Therapy (RMT)

Includes cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products, except for those regulated solely under section 361 of the Public Health Service Act …

Regenerative Medicine Advanced Therapy (RMAT) Designation

- To expedite the development and review of regenerative medicine advanced therapies
  - Applies to certain cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products
  - Genetically modified cell therapies and gene therapies producing durable effects included

Section 3033: Regenerative Medicine Advanced Therapy (RMAT) Designation

- Creates program for designation of regenerative medicine advanced therapies
- A drug is eligible for designation if:
  - It is a regenerative medicine therapy
  - The drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and
  - Preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition

Process for RMAT Designation

- Sponsor can make a request with a new IND submission or as an amendment to an existing IND

- Website with information about administrative process: http://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm537670.htm

Process for RMAT Designation

- Request for designation should describe:
  - How the drug meets the definition of regenerative medicine therapy
  - How the drug meets the criterion that it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and
  - The preliminary clinical evidence that indicates that the drug has the potential to address unmet medical needs for such disease or condition

Process for RMAT Designation

- FDA has 60 calendar days to determine if designation criteria are met
  - FDA will provide written response
  - If not granted, FDA will provide a written description of the rationale

Benefits of RMAT Designation

- Interactions with FDA to expedite development and review of regenerative medicine advanced therapies
  - Benefits available to breakthrough therapies
  - Including early discussions of any potential surrogate or intermediate endpoints to support accelerated approval

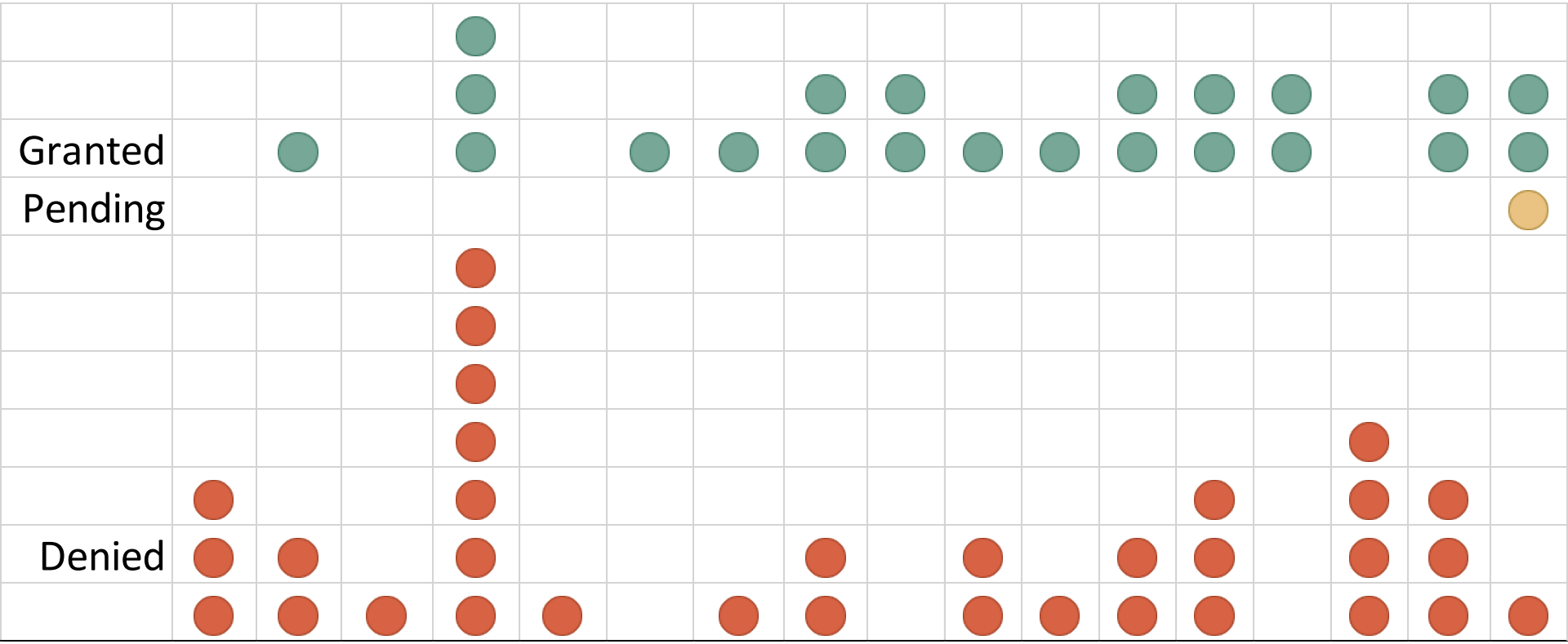
Benefits of RMAT Designation (cont'd.)

- May be eligible for priority review
- May be eligible for accelerated approval, as agreed upon during product development, based on:
  - Surrogate or intermediate clinical endpoints reasonably likely to predict long-term clinical benefit, or
  - Reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites, as appropriate

Accelerated Approval for RMATs

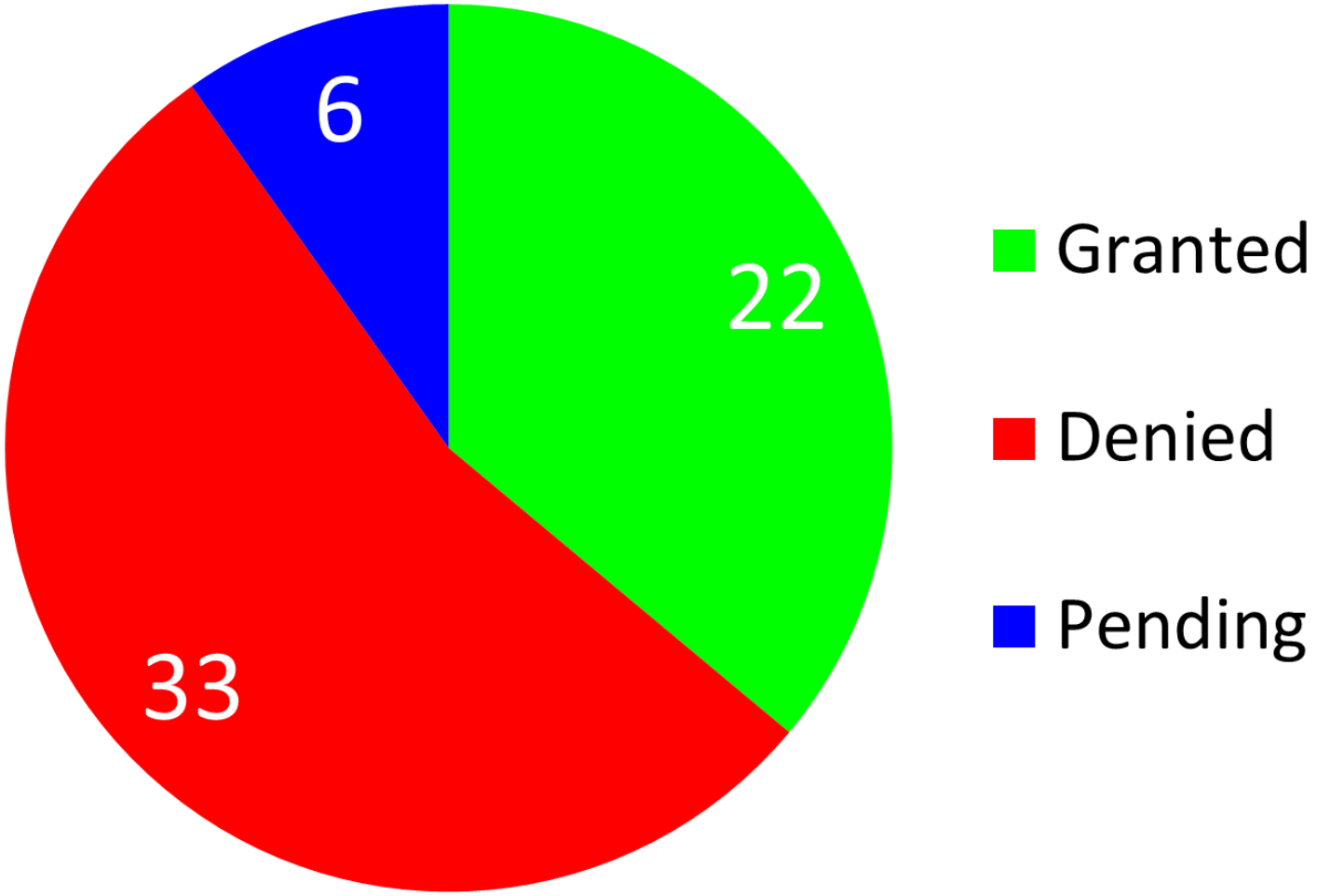
- If accelerated approval is granted, post-approval requirements may be fulfilled through:
  - Post-approval clinical studies
  - The submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence such as electronic health records, or
  - The collection of larger confirmatory data sets as agreed upon during product development, or
  - Post-approval monitoring of all patients treated with such therapy prior to approval of the therapy

RMAT Designation Requests Status
- as of June 12, 2018



12/13/2016 – 06/12/2018

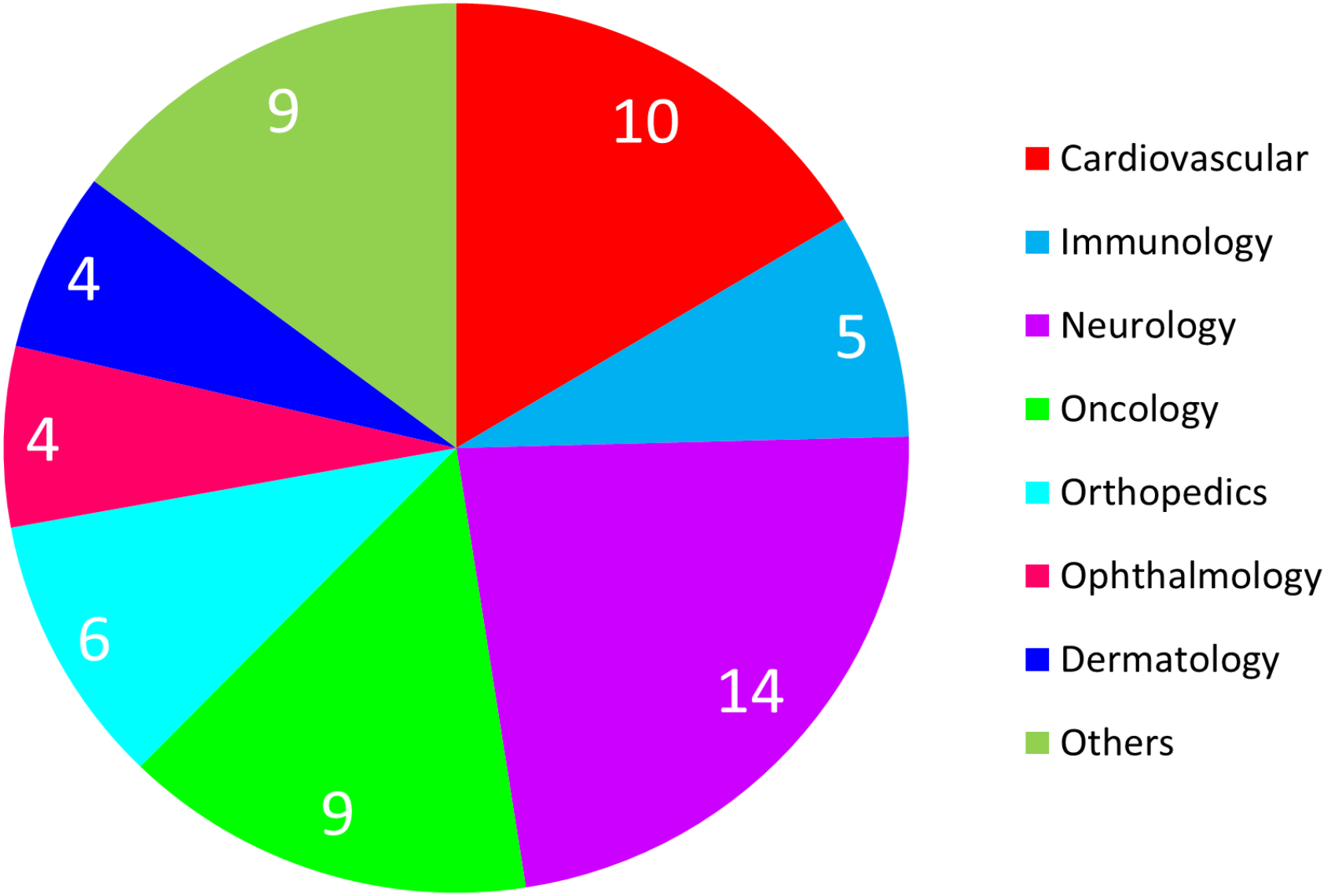
RMAT Designation Requests Status - as of June 12, 2018



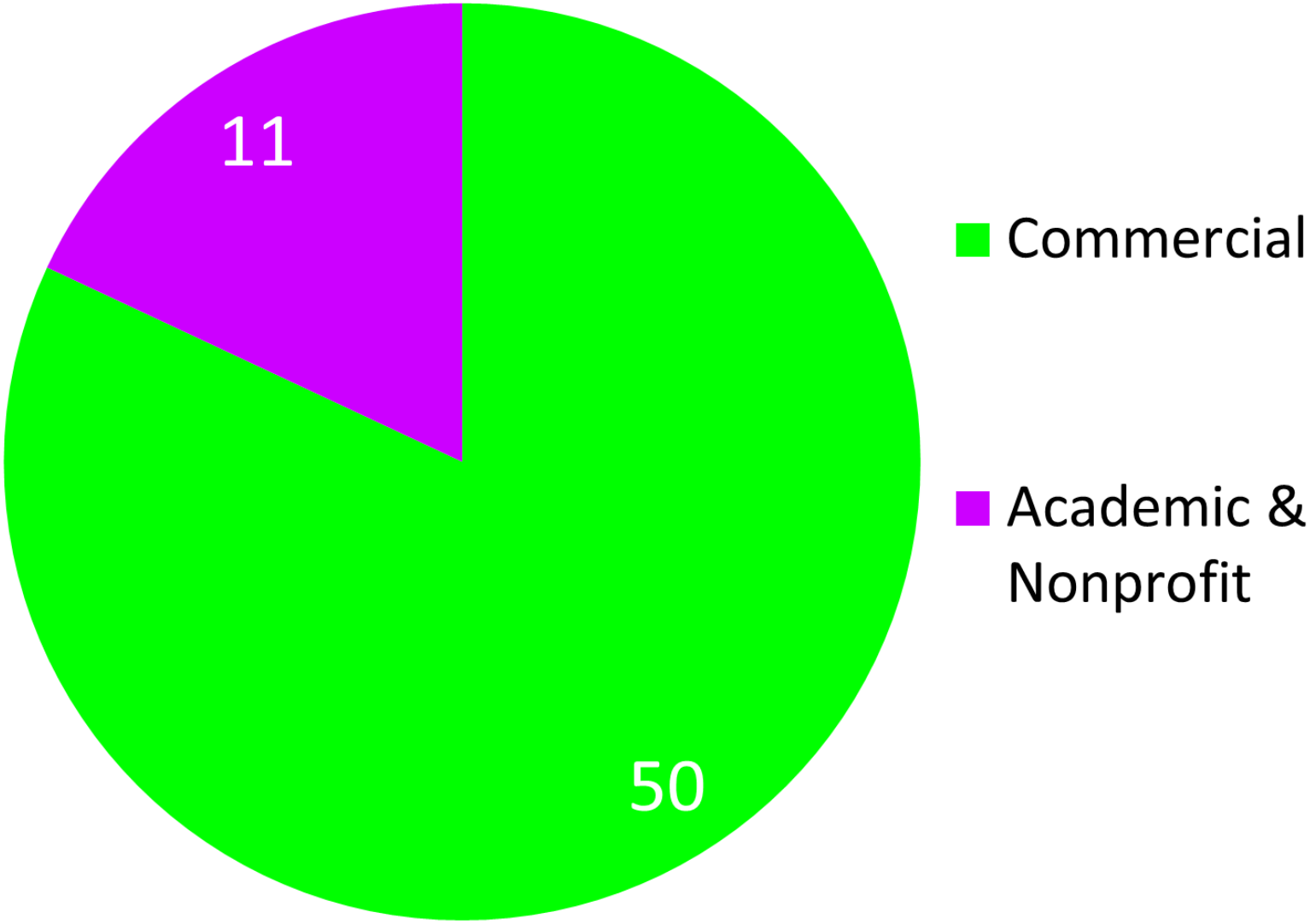
Analysis of Denied Regenerative Advanced Therapy Designation Requests

- Administrative Reasons
  - Inactive IND
  - No preliminary clinical evidence submitted
- CMC Reasons
  - Different product
- Insufficient Preliminary Clinical Evidence
  - Study design issues
  - Inconsistent results with regard to product activity

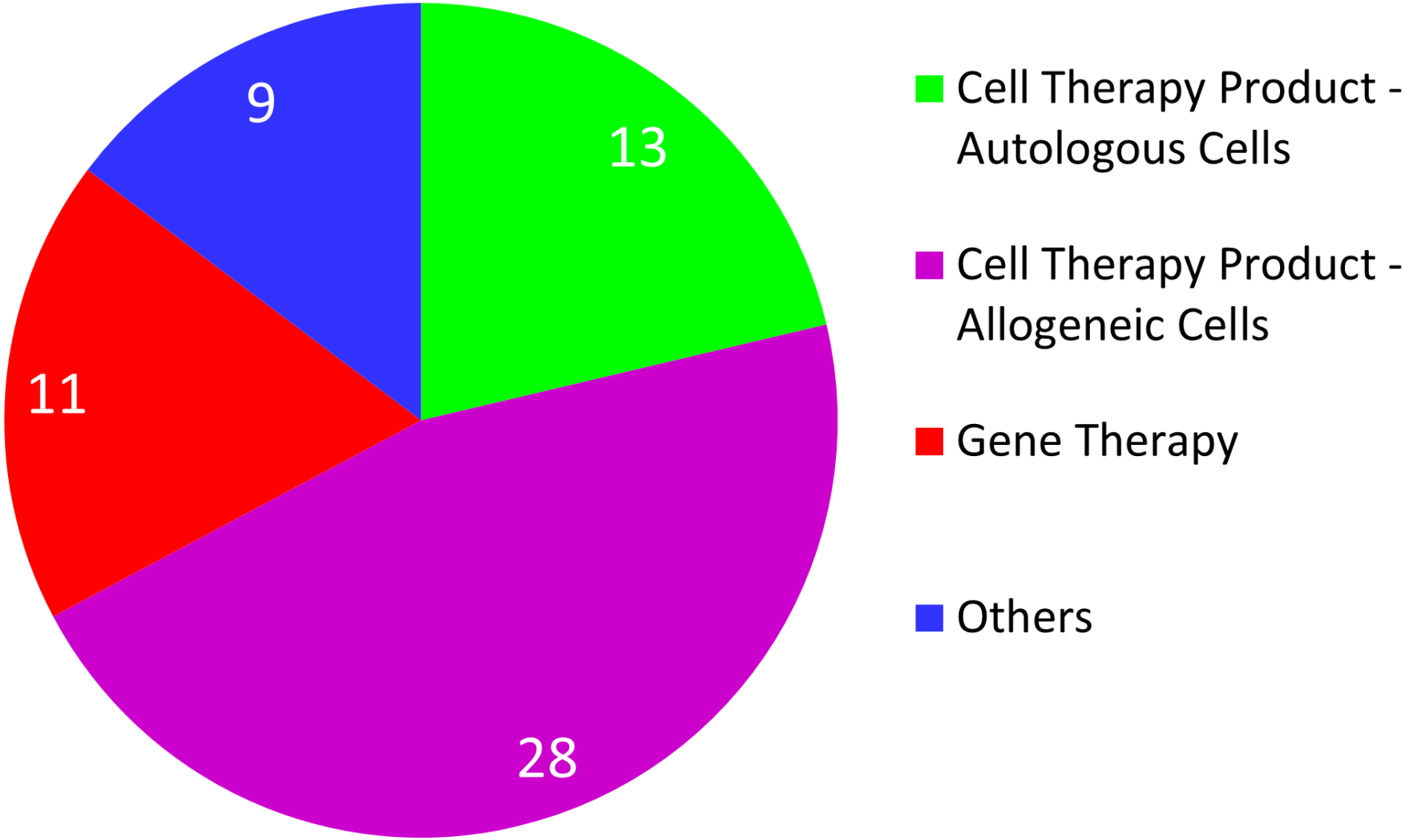
RMAT Designation Requests
- Distribution by Specialty



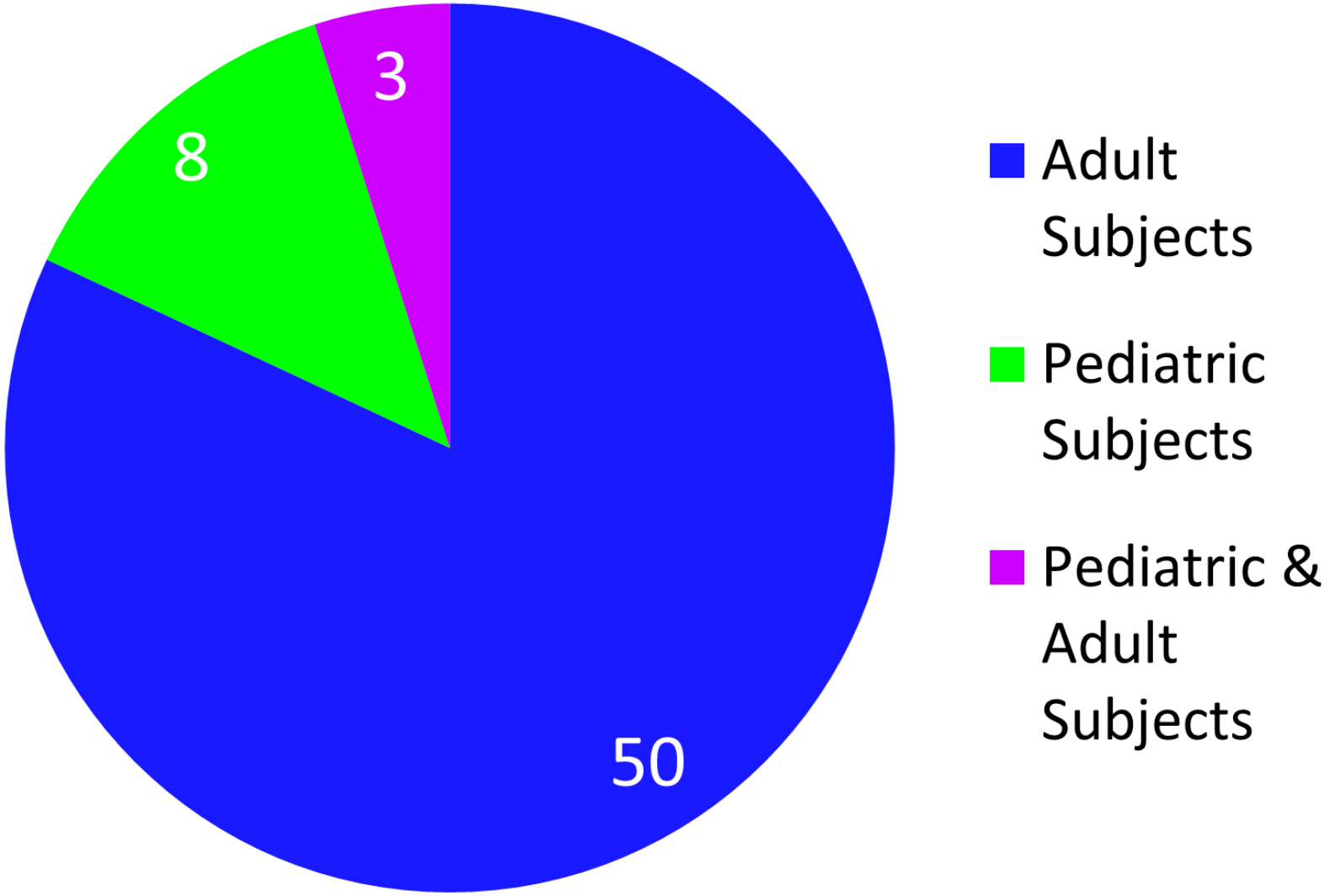
RMAT Designation Requests
- Distribution by Applicant



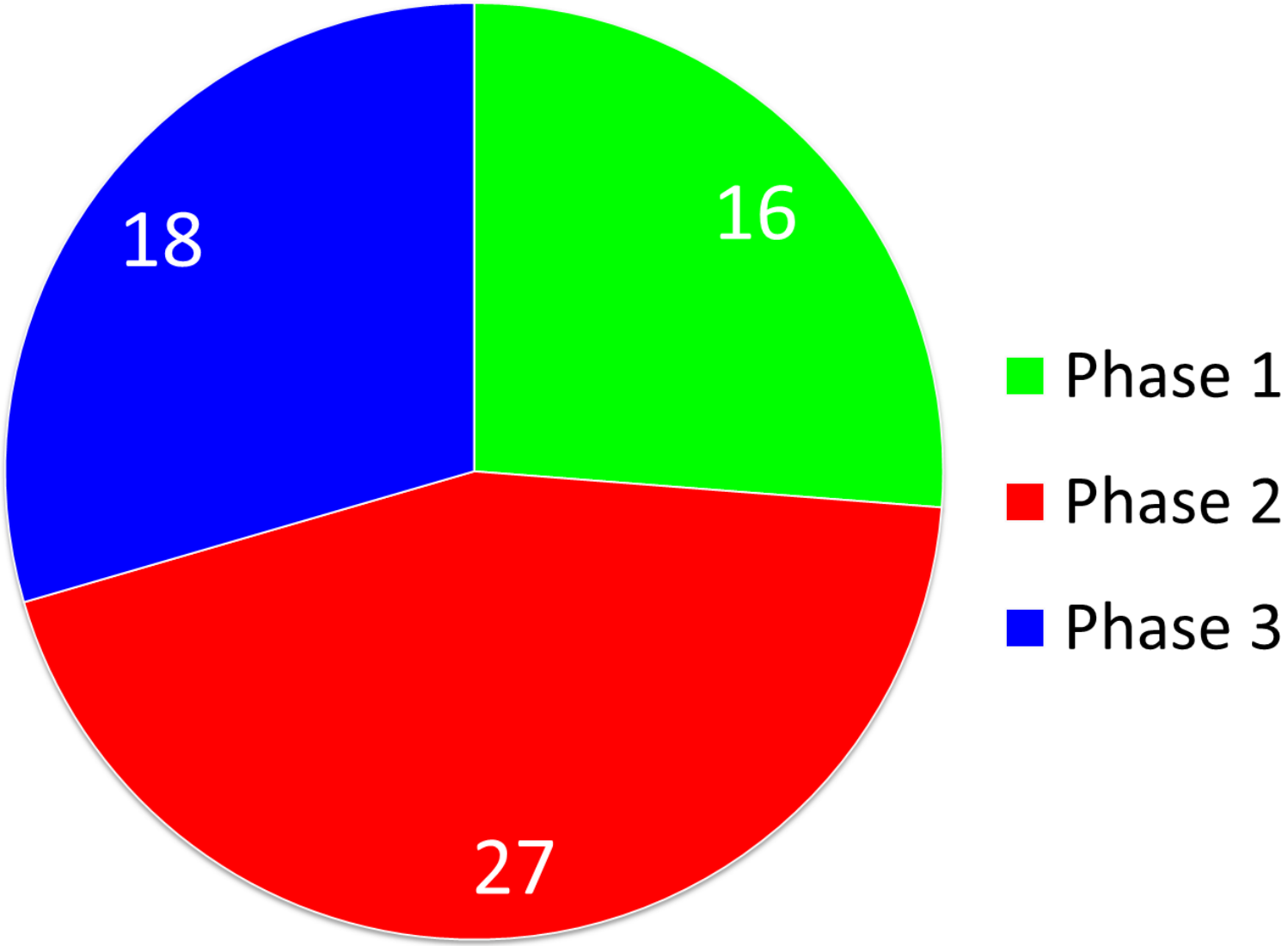
RMAT Designation Requests
- Distribution by Product Type



RMAT Designation Requests
- Distribution by Study Population



RMAT Designation Requests
- Distribution by Current Study Status



2017 FDA Guidances in Regenerative Medicine

- Expedited Programs for Regenerative Medicine Therapies for Serious Conditions; Draft Guidance for Industry
- Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use; Guidance for Industry and Food and Drug Administration Staff
- Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception; Guidance for Industry
- Evaluation of Devices Used with Regenerative Medicine Advanced Therapies; Draft Guidance for Industry

Contact Information

- **Regulatory Questions:**

  OTAT Main Line – 240 402 8190

  Email: OTATRPMS@fda.hhs.gov and

  Lori.Tull@fda.hhs.gov

FDA Headquarters

- **OTAT Learn Webinar Series:**

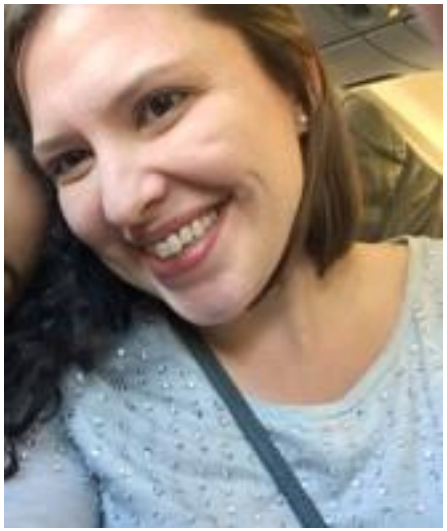
  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm

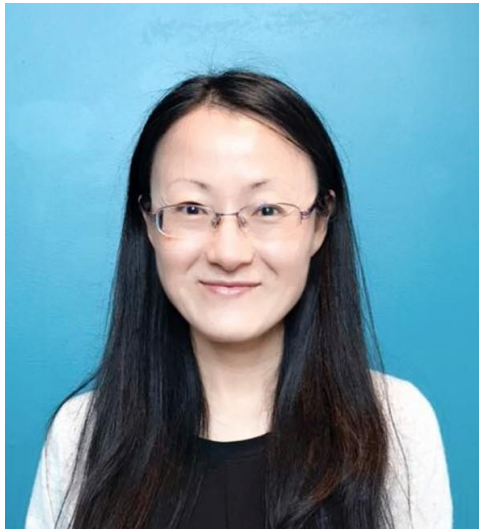
- **CBER website:** www.fda.gov/BiologicsBloodVaccines/default.htm
- **Phone:** 1-800-835-4709 or 240-402-8010
- **Consumer Affairs Branch**: ocod@fda.hhs.gov

- **Manufacturers Assistance and Technical Training Branch**: industry.biologics@fda.hhs.gov
- **Follow us on Twitter:** https://www.twitter.com/fdacber

Acknowledgements

- Rachael Anatol, PhD
- Xiaofei Wang, PhD





Contact Information

Wilson W. Bryan, M.D.

wilson.bryan@fda.hhs.gov

Regenerative Medicine Advanced Therapy (RMAT) Designation

International Cord Blood Symposium (ICBS)
San Diego, California
June 14, 2018

Wilson W. Bryan

Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)
United States Food and Drug Administration (US FDA)

21st Century Cures Act: Title III, Sections 3033-3036

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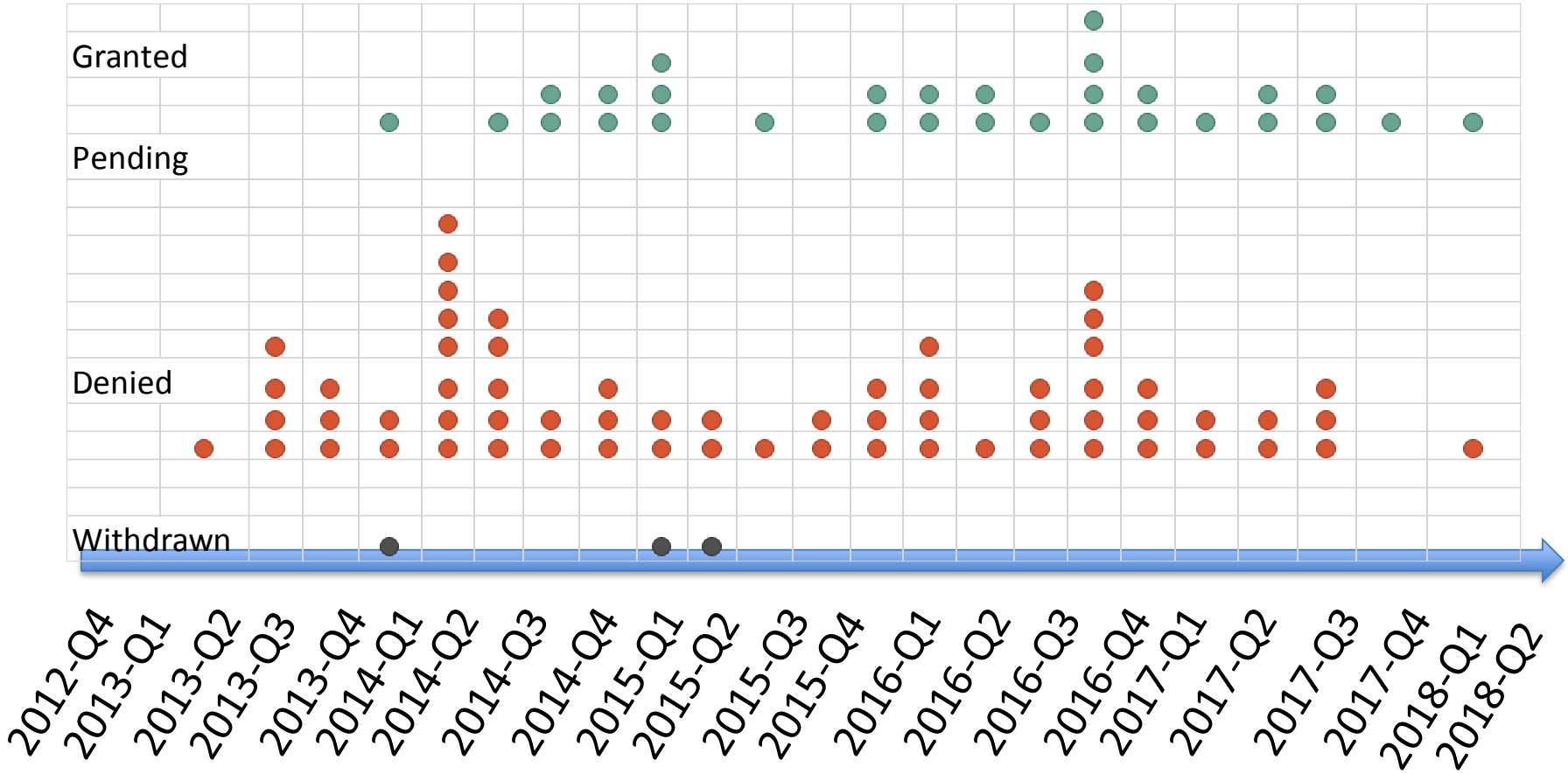
Section 3034: Guidance Regarding Devices Used in the Recovery, Isolation, or Delivery of Regenerative Medicine Advanced Therapies (RMATs)

- Requires FDA to issue draft guidance by December 2017
- Directs guidance to specifically address:
  - How FDA intends to simplify and streamline regulatory requirements for combination device and cell or tissue products
  - What, if any, intended uses or specific attributes would result in a device used with a regenerative therapy product being classified as a class III device
  - When FDA considers it necessary, if ever, for the intended use of a device to be limited to a specific intended use with only one particular type of cell, and,
  - Application of the least burdensome approach to demonstrate how a device may be used with more than one cell type

Section 3036: Standards for Regenerative Medicine Therapies (RMTs) and Regenerative Medicine Advanced Therapies (RMATs)

- In consultation with the National Institute of Standards and Technology (NIST) and stakeholders, FDA will facilitate an effort to coordinate and prioritize the development of standards and consensus definition terms
  - Identify opportunities to help advance development of regenerative medicine therapies and regenerative medicine advanced therapies
  - Identify opportunities for the development of laboratory regulatory science research and documentary standards
  - Work with stakeholders in the development of such standards

BT Designation Requests Status
- as of June 12, 2018



BT Designations by Disciplines*

Indications	Requests	Granted
Oncology (Solid Tumor)	34	6
Hematology (Malignant and Benign)	26	16
Non-Onco/Hema	33	8

*Excluding withdrawn and pending requests

BT Designations by Product Types*

Products	Requested	Granted
Gene Therapy	48	23
Cell Therapy	26	3
Others	19	4

*Excluding withdrawn and pending requests