
ALLIANCE for
Regenerative Medicine

WEBINAR

Understanding the
21st CENTURY CURES ACT
FOR CELL & GENE THERAPIES

FEB 2, 2017

ALLIANCE for Regenerative Medicine

Agenda

Introduction & Current State of Affairs
Presented by: Michael Werner, Alliance for Regenerative Medicine

CBER Reorganization & Regenerative Advanced Therapies
Presented by: Wilson W. Bryan, M.D. & Rachael F. Anatol, Ph.D., FDA's Center for Biologics Evaluation and Research, Office of Tissues and Advanced Therapies

Industry Perspective
Presented by: Anne-Virginie Eggimann, bluebird bio

Michael Werner

Executive Director

Alliance for Regenerative Medicine

ALLIANCE for Regenerative Medicine

About the Alliance For Regenerative Medicine

The Alliance for Regenerative Medicine (ARM) is the preeminent global advocate for regenerative and advanced therapies. ARM fosters research, development, investment and commercialization of transformational treatments and cures for patients worldwide.

By leveraging the expertise of its membership, ARM empowers multiple stakeholders to promote legislative, regulatory and public understanding of, and support for, this expanding field.

Current State of Affairs in Washington

Trump Administration View of Life Sciences

- *Executive order on regulatory oversight unknown*
  - *FDA not participating in user fee discussions with Congress*
- *"Drug industry is getting away with murder"*
  - *Trump has supported Medicare negotiations with drug companies on prices*
- *Hiring freeze on federal level could potentially impact FDA resources*

Current State of Affairs in Washington

Key Government Officials

- HHS Secretary Designee Tom Price
  - Orthopedic surgeon. Strong opponent of Affordable Care Act. Supports greater use of Health Spending Accounts and Medicaid reforms. Friend of drug and biotech industry. FDA critic.
- Proposed CMS Administrator Seema Verda
  - State Medicaid consultant with close ties to Vice President Pence. Likely to support State waivers and other flexibility proposals, including other reforms such as block grants or per capita payments.
- FDA Commissioner – President Trump: FDA head to be named "fairly soon"
  - Jim O'Neill – Mithril Capital Management. Has advocated that FDA pre-market review should be for safety only; efficacy demonstrated post-approval.
  - Scott Gottlieb, MD – Former senior FDA and CMS official in Bush Administration. Clinical assistant professor at New York University School of Medicine.
  - Jack Kalavitrinios – Head of HHS "landing party" for Trump. Formerly at Covidien.
  - Joseph Gulfo, MD – Former CEO of drug and device companies with medical background and experience working with FDA on product approvals. Author of "Innovation breakdown: How the FDA and Wall Street cripple medical advances."
  - Balaji Srinivasan – CEO of bit coin startup21.co.

ARM's Policy Goals/Objectives

Heading into the Cures debate, ARM had 4 goals:

- *Explicit recognition of the potential of RM/AT products to treat, modify, reverse, or cure serious or life-threatening diseases and conditions and therefore special provisions*
- *An improved approval pathway that helps safe and effective RM products reach patients as soon as possible and maintains high FDA product approval standards*
- *Get federal support for standards efforts, especially the Standards Coordinating Body*
- *Opposition to proposals that would weaken FDA standards or not fully ensure that safe and effective products reached the market*

Goals Accomplished: 21st Century Cures Act Was A Major Win

21st Century Cures Act benefits patients and the RM/AT sector:

- *Explicitly recognizes the potential of RM/AT products to treat, modify, reverse, or cure serious or life-threatening diseases and conditions*
- *Optimizes approval pathway & maintains high FDA product approval standards*
  - *Guaranteed interactions with FDA*
  - *Eligibility for priority review & accelerated approval*
  - *Flexibility in number of clinical sites used with possibility of using patient registry and other "real world" evidence for post-approval studies*
- *Directs HHS/FDA to work with industry & other stakeholders to create RM standards*
- *Addresses concerns with REGROW Act whose provisions would put patients at risk and hurt product development by reducing FDA's regulatory standards*

ARM's Contribution to 21st Century Cures

ARM served as the "hub of the wheel" among key stakeholders:

- *Engaged in years-long legislative dialogue with bipartisan congressional offices, FDA, White House, patient advocacy organizations, media, industry trade associations, other organizations, etc.*
- *Facilitated creation of international Standards Coordinating Body for regenerative medicine in collaboration with scientific organizations, accrediting bodies, federal agencies, standard setting organizations, other organizations*
- *Hosted discussions, panels at seminars and conferences, etc.*

ARM and more than 25 Charter Members launched RM Standards Coordinating Body on January 18, 2017

- *SCB is organizing industry and standards dev. organization participation in standards development activities described in 21st Century Cures*
- *MoU with NIST signed last year to create a public-private partnership that will enable close coordination with NIST, FDA, NIH, DoD and other federal agencies*
- *Work plans under development in four technology areas to identify most immediate needs: Cell therapy (initial projects approved), gene therapy (including gene editing), tissue engineering, and cell-based drug discovery*
- *Enables industry support of ISO RM standards setting efforts led by NIST*

FDA U.S. FOOD & DRUG ADMINISTRATION

CBER Reorganization and Regenerative Advanced Therapies

Wilson W. Bryan, MD
and
Rachael Anatol, PhD

February 2, 2017

Outline

- Office update
- 21st Century Cures regenerative medicine provisions
- Resources

FDA Organization

- **CBER (Center for Biologics Evaluation and Research)**
  - **vaccines, blood products, allergenic products, human tissue/tissue products for transplantation, cells, gene therapy, some devices (related to blood and HCT/Ps)**
- **CDER (Center for Drug Evaluation and Research)**
  - **drugs, some biological products**
- **CDRH (Center for Devices and Radiological Health)**
  - **Most devices (including for treatment, implants, diagnostics)**

Effective October 16, 2016

- **Name change: Office of Tissues and Advanced Therapies (OTAT)**
- **All of Office of Cellular, Tissue, and Gene Therapies (OCTGT) is now part of OTAT**
- **Transfer of some products from Office of Blood Research and Review (OBRR) to OTAT**
- **Two Divisions in OBRR have transferred to OTAT**
  - **Division of Hematology Clinical Review**
  - **Division of Hematology Research and Review**
- **Products for transfusion remain in OBRR**

OTAT Products

- Stem cell and stem cell-derived products
  - Hematopoietic, mesenchymal, cord blood, embryonic, iPSCs
- Somatic cell therapies
  - Pancreatic islets, chondrocytes, myoblasts, keratinocytes, hepatocytes
- Therapeutic vaccines and other antigen-specific active immunotherapies
  - Cancer vaccines and immunotherapies, such as dendritic cells, lymphocyte-based therapies, cancer cell-based therapies, peptides, proteins
  - Non-infectious disease therapeutic vaccines, such as peptides, proteins, small molecules

OTAT Products, Cont'd.

- Gene therapies
  - Genetically modified cells
  - Plasmids, viral vectors, bacterial vectors
- Purified and recombinant proteins for hematology (e.g., coagulation factors, thrombin, botulism antitoxin, diphtheria anti-toxin, fibrin sealants)
- Antivenins
- Some devices and combination products
  - Devices with a cellular component
  - Selection devices for the manufacture or delivery of cells

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

- Regenerative medicine provisions:
  - Section 3033: Creates program for designation of regenerative 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

Section 3033: Accelerated Approval for Regenerative Advanced Therapies

- Creates program for designation of regenerative advanced therapies
- A drug is eligible for designation if:
  - It is a regenerative medicine therapy (cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products)
  - 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

Benefits of Regenerative Advanced Therapy Designation

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

Benefits of Regenerative Advanced Therapy 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 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 Regenerative Advanced Therapy Designation

- 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

Process for Regenerative Advanced Therapy 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 Regenerative Advanced Therapy 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 Regenerative Advanced Therapy 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

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

- 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 3035: Report on Regenerative Advanced Therapies

- Before March 1 each year, FDA will report to Congress with respect to the previous calendar year:
  - The number and type of applications for approval of regenerative advanced therapies filed, approved or licensed, withdrawn, or denied, and
  - How many such applications were granted accelerated approval or priority review

Section 3036: Standards for Regenerative Medicine and Regenerative Advanced Therapies

- 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 advanced therapies
  - Identify opportunities for the development of laboratory regulatory science research and documentary standards
  - Work with stakeholders in the development of such standards

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Public access to CBER

- **CBER website:**
  http://www.fda.gov/BiologicsBloodVaccines/default.htm
  Phone: 1-800-835-4709

- **Consumer Affairs Branch (CAB) Email: ocod@fda.hhs.gov**

- **Manufacturers Assistance and Technical Training Branch (MATTB) Email: industry.biologics@fda.gov**

- **Follow us on Twitter**
  https://www.twitter.com/fdacber

OTAT contact information

- **Regulatory Questions**:
  Contact the Regulatory Management Staff in OCTGT at CBEROCTGTRMS@fda.hhs.gov or Ramani.Sista@fda.hhs.gov

- **References for the regulatory process for OTAT**
  - **http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/OtherRecommendationsforManufacturers/ucm094338.htm**

- **OTAT Learn Webinar Series:**
  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm

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Anne-Virginie Eggimann

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bluebird bio

Industry Perspective

- *Regenerative advanced therapy designation highlights key concepts that are relevant for efficient development of tissue & cell-based products*
- ***Early multidisciplinary discussion** with FDA Office of Tissues & Advanced Therapies (OTAT) on **evidence generation plan** and potential for accelerated approval via use of **surrogate** or **intermediate endpoints** or data from **limited number of clinical sites***
  - *As soon as "preliminary clinical evidence" is available to address unmet need; at the time of IND filing or shortly thereafter*
- *Clear potential for eligibility to benefit from **priority review** & **accelerated approval***
- *Outlines options for post-approval requirements & includes possibility to use **real world evidence** (patient registries, health electronic records, etc.)*
- *Clarifies regulatory pathway building on existing regulatory tools*

Next Steps

- *Work with FDA on implementation as appropriate*
  - *http://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm537670.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery*
- *Get clarity and secure explicit inclusion if necessary of gene therapy into the definition of regenerative advanced therapy.*
  - *Staff indicated that ex vivo gene therapy would be included*

Questions?

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