FDA U.S. FOOD & DRUG ADMINISTRATION

# Variability of Regenerative Engineering Products and the Regulatory Approval Pathway

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Forum on Regenerative Medicine

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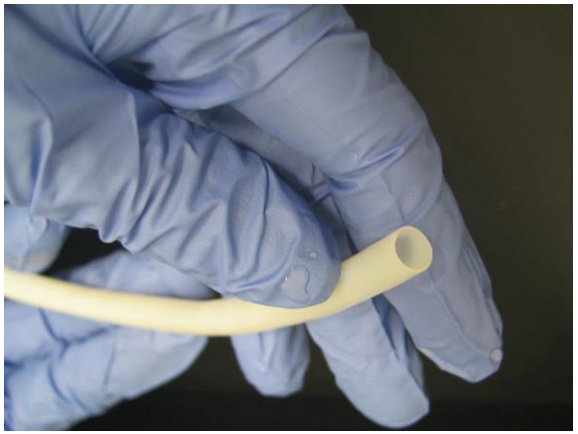
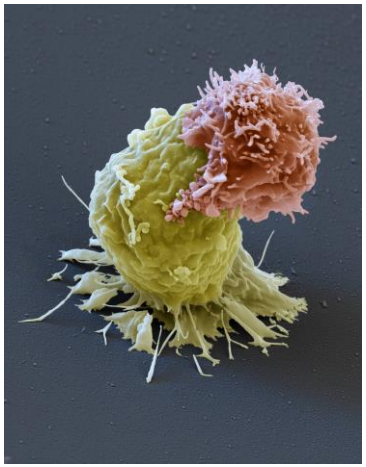
# Regenerative Medicine: Variety of Products

Bioengineered skin



Bioengineered blood vessel

Bioengineered bladder



Chimeric antigen receptor-T cell
(in red attacking cancer cell in yellow)

# Sources of Variability Potentially Affecting Regulatory Approval

- Donor pretreatment
- Cell or tissue identity
- Manufacturing steps
- Preparative regimen in recipient
- Clinical trial inclusion and exclusion criteria
- Endpoint assessment
- Disease outcome

# Expedited Programs for Regenerative Medicine Therapies – Draft

- Describes FDA's considerations in implementing the Regenerative Medicine Advanced Therapy Designation (RMAT) to expedite product development and review
  - 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

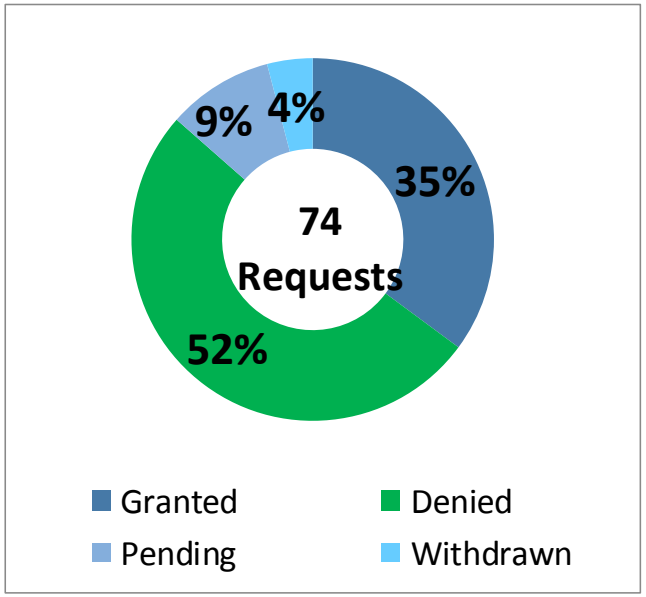
# Regenerative Medicine Advanced Therapy Designation (RMAT)

- Products must be intended for serious or life-threatening diseases or conditions
- Preliminary clinical evidence must indicate potential to address unmet medical needs
- FDA will reply to submitted designation requests with 60 days
- Designated products are eligible as appropriate for priority review and accelerated approval

# RMAT Accelerated Approval Provisions

- Post-approval requirements can be fulfilled as appropriate through submission of
  - Clinical evidence, clinical studies, patient registries or other sources of real world evidence such as electronic health records
  - Collection of larger confirmatory datasets as agreed upon
  - Post-approval monitoring of all patients treated with such therapy prior to approval of the therapy

# RMAT Designations Granted




Data as of August 30, 2018

- 26 products granted designation
- 17/26 products have Orphan Product designation
- Most are cellular therapy products or cell-based gene therapy products

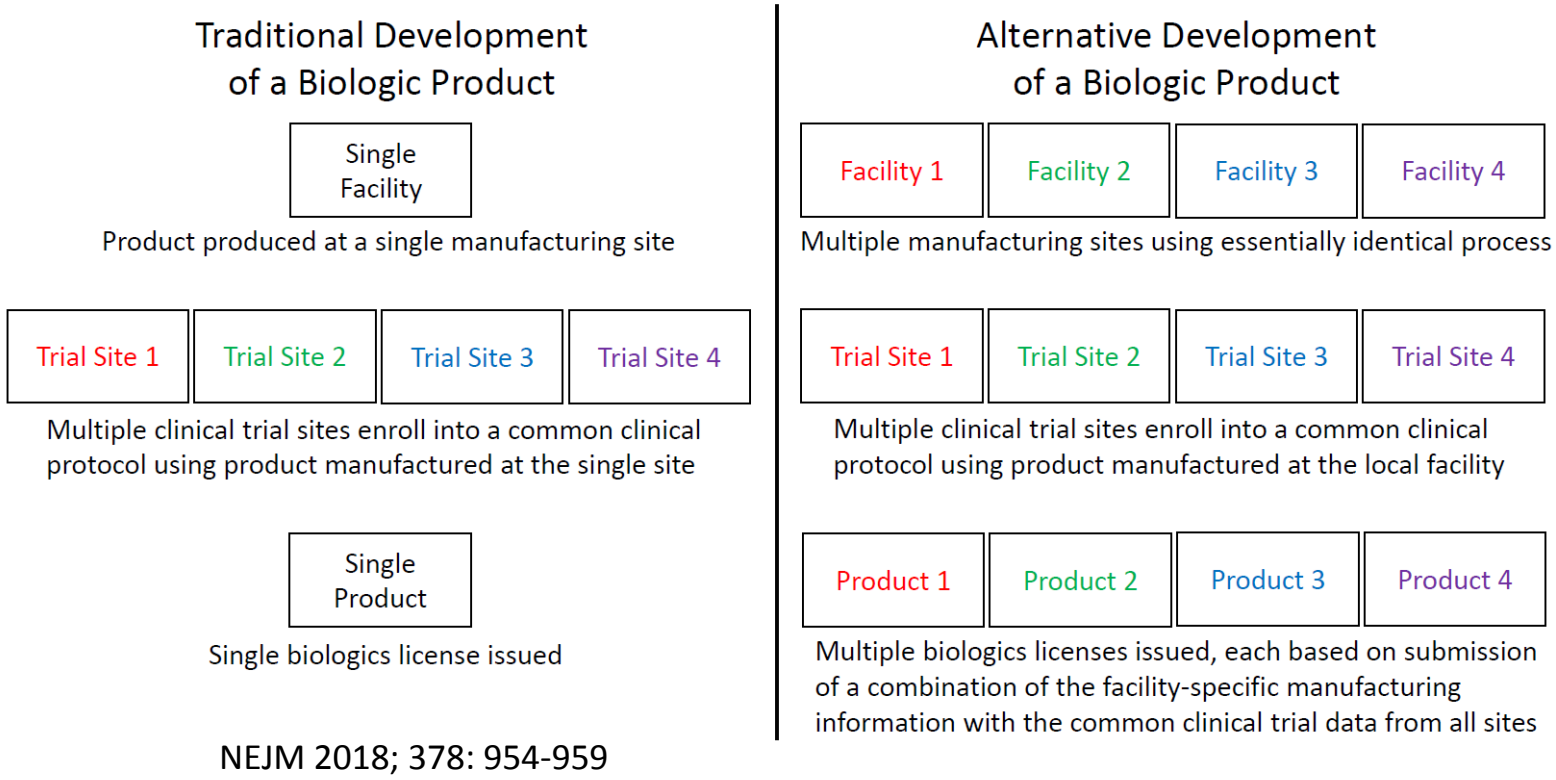
# Challenges in the Development of Regenerative Medicine Therapies

- Need for standards for the reproducible production of regenerative medicine products
  - Collaboration with National Institute of Standards and Technology (NIST)
  - Standards Coordinating Body
- Transition from pilot scale to commercial manufacturing can be challenging
  - Distributed versus centralized manufacturing
  - Consider scalable manufacturing processes

# Challenges in the Development of Regenerative Medicine Therapies

- Need novel approaches to clinical development to address complex therapies and small patient populations
  - Develop integrated development plans
  - Collaborative development is sometimes possible

# Innovative Development Program for Regenerative Medicine Products



# Resources for Product Development

- Sponsors are encouraged to contact the Office of Tissues and Advanced Therapies early on to discuss plans for development
  - INTERACT program (INitial Targeted Engagement for Regulatory Advice on CBER producTs)
  - Email industry.biologics@fda.hhs.gov
- Useful information for product developers can all be found on FDA's website www.fda.gov

# Summary

- FDA is committed to advancing the development and evaluation of regenerative medicine products
  - Helping to individualize product development
  - Working to overcome limitations in manufacturing
  - Providing input and collaboration on novel endpoints
  - Encouraging innovative clinical trial designs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