



# FDA Approach to the Regulation of Hematopoietic Stem/Progenitor Cells (HPC)

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# FDA proposed approach to regulation of cell and tissue products

- Announced February 1997
- Risk-based approach - broad range of products
- Level and type of regulation commensurate with the risk posed by the product
- Like products should be treated alike
- FDA exercises regulatory oversight only to degree appropriate to protect public health

# FDA's Proposed Approach

Regulatory framework has three main goals

1. Prevent unwitting use of contaminated tissues with the potential for transmitting infectious disease
2. Prevent improper handling or processing that might contaminate or damage tissues
3. Ensure that clinical safety and effectiveness is demonstrated for most tissues that are highly processed, used for non-natural purposes, combined with non-tissue components, or that have systemic effects on the body

# How are HPC regulated within this framework?

- HPC from cord blood and peripheral blood are “human cells, tissues, or cellular or tissue-based products” (HCT/P)
- Regulations at 21 CFR Part 1271 apply to all HCT/P, including HPC
- Certain HPC are subject to additional regulation, including GMP and biological product licensing requirements

# Two Main Regulatory Tiers

- Regulated solely under HCT/P regulations if *ALL* “kick down” factors apply
  - Authority derived from Section 361 of the PHS Act
- Regulated under HCT/P regulations *AND* premarket review, etc. if product does not meet all “kick down” factors
  - Authority derived from FFDCA and PHS Act, sections 351 and 361

# “Kick down” Factors

## 21 CFR 1271.10(a)

- Minimally manipulated
- Intended for homologous use only
- Not combined with drug, device, or biologic
  - Exceptions: sterilizing, preserving, storage agents that do not raise new safety concerns
- Does not have systemic effect
  - Exceptions: autologous use, use in first or second degree family relative, reproductive use

# Which HPC are regulated as biological products?

- All ***allogeneic, unrelated*** HPC from cord and peripheral blood
- HPC (and bone marrow) that are ***more than minimally manipulated***
  - Examples: expanded, activated, genetically modified
- HPC (and bone marrow) that are ***combined with a drug, device or biologic***
- HPC (and bone marrow) that are intended for ***non-homologous use***
  - Example: HPC for cardiac repair

# Which HPC are currently subject to IND/BLA requirements?

- HPC and bone marrow that are:
  - More than minimally manipulated; OR
  - Intended for non-homologous use; OR
  - Combined with drug, device, or biologic



# Which HPC are subject to phase-in of FDA approval requirements?

- Allogeneic unrelated minimally manipulated HPC for homologous use are subject to biological product requirements, including licensure
- However, FDA is not enforcing IND/BLA requirements for these HPC pending development of a regulatory approach to licensure

# Request for Standards

- Request for Proposed Standards for Unrelated Allogeneic Peripheral and Placental/Umbilical Cord Blood HPCs; Request for Comments (Federal Register - January 1998)
  - Applies only to unrelated allogeneic minimally manipulated HPC for hematopoietic reconstitution
  - Requested submission of comments
    - Establishment controls
    - CMC controls
    - Processing & product standards
- Data received in docket for cord blood: Draft guidance published January 2007

# Regulations applicable to all HPC

## 21 CFR Part 1271

<b>Regulation Subparts</b>	<b>Proposed</b>	<b>Final *Effective date</b>
Establishment Registration and Product Listing	1998	2001 *2001 for some establishments *2004 for newly regulated tissues
Donor Eligibility	1999	2004 *May 2005
CGTP; Inspection and Enforcement	2001	2004 *May 2005

# Other regulations applicable to HPC under IND

- 21 CFR Part 312 - Investigational New Drug (IND) Application
- 21 CFR Parts 210/211 - Good Manufacturing Practice and statutory CGMPs (i.e., FDC Act)
- 21 CFR Parts 50 (protection of human subjects) and 56 (institutional review boards)

# Other regulations that would apply to licensed HPC

- 21 CFR Part 201—Labeling
- 21 CFR Part 202—Advertising
- 21 CFR Part 210/211—Good Manufacturing Practice
- 21 CFR Part 600—Biological Products; General (includes Reporting of Adverse Experiences and Biological Deviations)
- 21 CFR Part 601—Licensing
- 21 CFR 610—General Biologics Standards

# Considerations for unrelated allogeneic HPC, A

- Subject to IND and licensure requirements
  - Numerous (>100) donor centers involved
  - HPC, A often requires limited manufacturing beyond recovery, testing, labeling, distribution
  - Post-recovery manufacturing steps may be performed in laboratory at transplant center
  - Most HPC, A manufacturing performed by establishments participating in the NMDP registry
  - Other issues: Donor mobilization, cell selection/depletion, DLI
- Topic of advisory committee discussion 3/07