

# **Overview of Regulations and Standards for Cell Therapy: An International Perspective**

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# Cell Therapy Regulations Worldwide



- **Trend towards establishment of risk-based systems for regulation of cell therapy products - USA, Canada, Australia, EU and European nations.**
- **Multinational Guidelines, Standards, Regulations**
  - **World Health Organization (WHO)**
  - **International Conference of Harmonization (ICH)**
  - **European Commission, European Medicines Agency (EMA)**
  - **Council of Europe**
    - **Guide to safety and quality assurance for organs, tissues and cells**

# Regulations and Standards for Cell Therapy Products: North America

## USA

- FDA-CBER OCTGT, CDRH
  - GTPs, GMPs, GCPs
- FACT
- AABB
- AATB
- USP
- CAP, CLIA, JCAHO

## Canada

- Health Canada

# Regulations and Standards for Cell Therapy Products: Europe

- Evolving - centralized European regulatory authority and national regulatory agencies
- European Commission, European Medicines Agency (EMA)
  - Centralized approval pathway
- Federal regulatory agencies for each nation
  - Mutual Recognition approval pathway
  - Regulations and policy vary between nations
  - Cell therapy may be regulated as drug, device, biologic, or a combination of these, or specifically as cell therapy product
  - Manufacturing, labeling, oversight, approval requirements differ

# European Commission Directives 2001/83/EC and 2003/63/EC



- “Advanced therapy” products regulated as medicinal products, require premarket approval
  - Somatic cell therapy
  - Gene therapy
  - Xenotransplantation
  - *Regulation of tissue engineered products not specified*
- EMEA Committee for Medicinal Products for Human Use (CHMP, [www.emea.eu.int/htms/general/contacts/CHMP](http://www.emea.eu.int/htms/general/contacts/CHMP))
  - Cell-based Products Working Party (CPWP)
  - Gene Therapy Working Party (GTWP)

# European Commission Directive 2004/23/EC












- **Minimum quality and safety standards for donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.**
  - Donor selection, evaluation, informed consent
  - Traceability and adverse event reporting
  - GMP-based quality system
  - Data protection, confidentiality
- ***Each EU Member State can set more stringent requirements, or set policy regarding use of specific cell types***

# European Commission Directive 2006/17/EC








































- **Standards covering donation, procurement and testing of human cells and tissues**
  - Donor selection, medical history, testing, exclusion criteria for transmissible infectious diseases
  - Identification and traceability of donated cells or tissues
  - Facilities maintained to prevent contamination of tissues
  - SOPs for donation, testing, transport, receipt by tissue establishment
  - Personnel training
- **EU Member States to implement November 2006**

# Federal Regulation of Cell Therapy Products: Europe

-  Austria - Individual, not medicinal, products, GMPs required
-  France - Medicinal or cell therapy products, AFSSAPS, EFG regulate
-  Germany - Medicinal products, PEI regulates
-  Greece - Possibly medicinal products, status unclear
-  Ireland - Possibly medicinal products, determined case by case
-  Italy - Regulations emphasize transplantation, status of cell therapy products unclear
-  Spain - Biologics, drug, and device regulations may apply
-  Sweden - Generally considered medicinal product
-  UK - Medicinal products or medical devices

# “Patchwork” European Regulation of Tissue Engineered Products


													
		Austria	Belgium	Bulgaria	Finland	France	Germany	Ireland	Netherlands	Slovakia	Spain	Sweden	UK
<b>Framework</b>	None												
	Medicinal Product												
	Medicinal Product or Device												
	Specific guidance												
	Other regulations												
<b>Authorization</b>	Product Authorization												
	Manufacturing Authorization												
	Establishment Accreditation												
	Product and Mfg Authorization												

# European Commission - Proposed Regulation of Advanced Therapies



- Advanced therapies - somatic cell therapy, gene therapy, and tissue engineering
- Regulation intended address all advanced therapies, including tissue engineering, within an integrated framework
  - EMEA premarket approval required
    - Committee for Advanced Therapies
  - Demonstrate quality, safety, efficacy based on specific requirements
  - Risk management and long-term traceability

# Regulations and Standards for Cell Therapy Products: Australia

 Therapeutic Goods Administration (TGA) developing tiered, risk-based regulatory framework for cell and tissue therapies.

	<u>Good Tissue Practice Standards</u>	<u>TGA-Licensed Manufacturer, Relevant cGMPs</u>	<u>TGA Premarket Approval</u>
<b><u>Class 3</u></b> Not for direct transplant from donor to recipient, cells/tissue combined with device, produces metabolic effect <i>in vivo</i> , extensively manipulated	X	X	X
<b><u>Class 2</u></b> Not Class 3, and product is banked	X	X	
<b><u>Class 1</u></b> Not Class 2 or 3	X		

# Regulations and Standards for Cell Therapy Products: Asia

## Japan

- Ministry of Health, Labour and Welfare ([www.mhlw.go.jp](http://www.mhlw.go.jp))

## China

- State Food and Drug Administration of China ([www.sfda.gov.cn](http://www.sfda.gov.cn))

## Taiwan

- Bureau of Food and Drug Analysis ([www.nlfd.gov.tw](http://www.nlfd.gov.tw))
- BFDA 2006 International Symposium on Regulation of Human Cell and Tissue-Based Products, September 21-22, 2006, Taiwan

## India

- Central Drugs Standard Control Organization (<http://cdsco.nic.in/>)