Global regulatory framework for adult stem cell therapy: Systematic review

Jhyld C. Camacho[1], Lucas López Quiceno[1], Luz A. Palacio[1], Freddy A. Barrios[1], Kelly J. Rendon[1], Jose W. Martinez[1], Karolynn Halpert[1,2]
[1] Scientific Direction, Bioxcellerator, Medellín, Colombia.
[2] Chief Medical Officer, Bioxcellerator, Medellín, Colombia.

Background & Aim

According to scientific evidence, adult stem cell therapy is a safe and effective treatment for management of cardiovascular, neurological, autoimmune, ophthalmological, renal, hepatic and skeletal diseases; and could be a therapy for pathologies that lack specific treatment. However, most therapies are in experimental phase, and progress in research and clinical application depends on the regulatory systems of each country. Our aim is to perform an overview of global regulatory framework for adult stem cell therapy.

Methods

Systematic literature review on 28 websites of Regional Reference Regulatory Authorities according to Pan American Health Organization; in Asia, Europe, Americas, Oceania and other international organizations. 36 cell therapy regulations were included from 113,254 identified documents.

Results

Established regulation for cell banks, research and use in clinical practice of adult stem cell therapy is evidenced. See table 1.

International transverse principles regulate countries without a specific regulatory framework, such as European Union with Directive Law on Tissues and Cells 2004/23/EC and regulation 1394/2007.

Table 1. Legislative framework by region

Region	Country	Regulatory agency/entity	Title	Year	Type of approval	Type of cells/therapy/product
Asia	Japan	Pharmaceuticals and Medical Devices Agency – PMDA	Regulatory Trends in Regenerative Medicine in Japan	2013	Research and clinical practice	Human cells and tissues, and gene therapy products Advanced therapy drugs
			Pharmaceutical Products and Medical Devices Act (PMD Act)	2013	Production and commercialization of regenerative and cellular therapeutics	Cell- and tissue-based products, and gene therapy products
		Ministry of Health, Labour and Welfare	Act on the Safety of Regenerative Medicine	2013	Research and clinical practice	(1) technologies intended for reconstruction, repair or formation of structures or functions of human body or (2) those intended for treatment or prevention of human diseases
			Act on the Safety of Regenerative Medicine	2014	Production and marketing of cell regenerative and therapeutic products by companies	Human cells and tissues, and gene therapy products. 1. Bone marrow mesenchymal stem cells (MSC) for Graft-versus-host disease (normal approval) 2. Sheet of skeletal myoblasts for severe heart failure due to ischemic heart disease
	Korea	Ministry of Food and Drug Safety Corea (MFDS)	Law for the safety and support of advanced regenerative medicine and advanced biopharmaceuticals	2020	Clinical research and commercialization	Advanced regenerative medicine: Medical technology to treat, replace or regenerate damaged tissues and organs using human cells, etc. Advanced Biopharmaceuticals: Biopharmaceuticals (cell therapy products, gene therapy products, tissue engineering products, etc.)
Europe	European Union	European parliament and of the council	Directive 2004/23/EC of the European Parliament and of the Council	2004	Donation, obtaining, analysis, processing, conservation, storage, distribution, application and research	Hematopoietic stem cells from peripheral blood, umbilical cord, or bone marrow; reproductive cells, except in the aspects regulated in Law 14/2006, of May 26, on assisted human reproduction techniques; fetal cells and tissues, and adult and embryonic stem cells when their purpose is therapeutic use or clinical application.
	Germany	Federal Institute for Drugs and Medical Devices - BfArM	Law to ensure the protection of embryos in connection with the import and use of human embryonic stem cells (Stem Cell Law - StZG).	2007	Application	Advanced and gene therapies. Cellular therapy
		Federal Ministry of Justice and the Federal Office of Justice	Law to ensure the protection of embryos in relation to the importation and use of human embryonic stem cells (Stem Cell Law - StZG)	2002	Import and use of embryonic stem cells	Embryonic stem cell
	Austria	Federal Minister of Justice and the Federal Minister of Health and Women	Human Reproductive Technology Amendment Act of 2004	2004	Use in assisted reproduction	Embryonic stem cells for assisted reproduction
	Bulgaria	Health Minister	ORDINANCE No. 6 of March 5, 2007, on the approval of a medical standard for transplantation of organs, tissues and cells	2004	Use, collection and storage (including biobanks) of all human cells, organs and tissues	Human cells, organs and tissues
	Spain	Head of state	Law 14/2007, of July 3, on Biomedical Research	2007	Research and application for therapeutic purposes	Human stem cells
		State Agency. State official newsletter	Royal Decree-Law 9/2014, of July 4, which establishes the quality and safety standards for the donation, obtaining, evaluation, processing, preservation, storage and distribution of human cells and tissues; and the coordination and performance standards for use in humans are approved.	2014	Donation, obtaining, analysis, processing, conservation, storage, distribution, application and research	Hematopoietic stem cells from peripheral blood, umbilical cord, or bone marrow; reproductive cells, except in the aspects regulated in Law 14/2006, of May 26, on assisted human reproduction techniques; fetal cells and tissues, and adult and embryonic stem cells when their purpose is therapeutic use or clinical application.
		Ministry of Science and Innovation	Royal Decree 1527/2010, of November 15, which regulates the Commission of Guarantees for the Donation and Use of Human Cells and Tissues and the Registry of Research Projects	2010	Research and application for therapeutic purposes	Human stem cells
		Spanish Agency for Medicines and Health Products -AEMPS-	Royal Decree 477/2014, of June 13, which regulates the authorization of non-industrially manufactured advanced therapy drugs	2014	Application	Somatic stem cells
			Royal Legislative Decree 1/2015, of July 24, approving the consolidated text of the Law on guarantees and rational use of medicines and medical devices.	2015	Research	Somatic stem cells
			Guidelines of the Spanish Agency for Medicines and Health Products on the nomenclature of the active substances of medicinal products under investigation for advanced therapy that contain cells	2013	Research	Adult mesenchymal stem cells
	European Union UK	European Medicines Agency -EMA European parliament UK government	Regulation (CE) No1394/2007 of the European Parliament and of the Council of November 13, 2007, on advanced therapy medicinal products and by which Directive 2001/83/CE and Regulation (CE) No726/2004 are modified	2007	Storage, application and research	Human cells and tissues
	Finland	Ministry of Social Affairs and Health	Medical research law	1999	Research	Stem cells
	Grecia	Presidency of the Hellenic Republic	Presidential Decree 26/2008 - Official Gazette 51/A'/ 3.24.2008	2008	Storage (biobanks)	Stem cells
	Lithuania	Republic of Lithuania	Law of the Republic of Lithuania on the donation and transplantation of human tissues, cells and organs	1996	Storage and application for transplant purposes	Tissue cells (adult)
	Portugal	Assembly of the republic	Law no. 21/2014. Approval of clinical research	2014	Research	Somatic cells
	UK	UK government	Patentability of biotechnological inventions	2000	Application	Biotechnological inventions
		State secretary	Statutory Instruments 2007 No. 1523 The Human Tissue (Quality and Safety for Human Application) Regulations 2007.	2007	Storage and research.	Stem cells
	Czech Republic	Ministry of Health	About Research On Human Embryonic Stem Cells	2006	Research	Embryonic stem cells
Latin America	Argentina	Ministry of Health	Resolution No. 610/2007	2007	Research	Cells of human origin
		National central institute coordinator of ablation and implantation	Resolution no. 119.12 standards for good manufacturing and laboratory practices for cellular preparations	2012	Preparation and laboratory for cell preparations	Stem cells
	Brazil	National Health Surveillance Agency – ANVISA	Resolution of the collegiate board - RDC No. 505, of May 27, 2021	2021	Research	Advanced cell therapy and gene therapy
			Resolution of the collegiate board - RDC No. 506, of May 27, 2021	2022	Research	Advanced cell therapy and gene therapy
			Resolution of the collegiate board - RDC No. 508, of May 27, 2021	2023	Therapeutic use and research	I - hematopoietic progenitor cells, for conventional transplant purposes; II - Advanced Therapies Products; III - human cells that do not meet the conditions listed in art. 5 of this Resolution.
	Chile	Chamber of Deputies of Chile	Bulletin 11230-11. Modifies the health code in order to establish a legal framework to promote scientific research on stem cells and cell therapy.	2017	Research	Adult stem cells from umbilical cord blood, bone marrow, menstrual blood, skin, teeth, placental tissue, adipose tissue. Embryonic stem cells from human embryos or fetal tissue.
		Public Health Institute	Decree 3. Approves regulation of the national control system of pharmaceutical products for human use	2010	Registration, importation, importation and exportation, production, storage and possession, distribution	Biological products
	Colombia	National Institute for Drug and Food Surveillance -INVIMA-/ Congress of the republic	Project of law “by which the public and private banks of umbilical cord blood stem cells are regulated, and rules are established regarding their storage as an application of regenerative medicine. other provisions are directed”	2021	Stem cell banks, storage and application in regenerative medicine.	Cell therapy
	Latin American countries	Pan American Health Organization -PAHO-	Strategy and plan of action on donation and equitable access to transplantation of organs, tissues and cells 2019-2030	2019	Application	Cells, organs and tissues
	Mexico	COFEMERSIMIR	Official Mexican Standard Project NOM-260-SSA1-2015, for the disposal of stem and progenitor cells for therapeutic and research purposes	2015	Provision, therapeutic use and research	Human stem cells
North America	USA	Food and Drug Administration -FDA-	Title 21 of the Code of Federal Regulations (CFR) Part 1271: human cells, tissues, and cellular and tissue-based products	2001	Manufacture human cells, tissues, and cellular and tissue-based products (HCT/P's)	Human cells
			Section 351 of the PHS Act HCT/Ps minimally manipulated	2020	Marketing and use	Human cells

Conclusion

Regulatory agencies such as the FDA, EMA, PMDA and AEMPS have a completer and more up-to-date regulatory framework on adult stem cell therapy than others. In most Latin American countries, there are no regulations that regulate stem cell therapy for research and therapeutic use