Standards for Stem Cells and Regenerative Medicine

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Health Policies and Standards Department

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ACKNOWLEDGMENT

The Health Policy and Standards Department (HPSD) developed this Standard in collaboration with Subject Matter Experts and would like to acknowledge and thank these health professionals for their dedication toward improving quality and safety of healthcare services in the Emirate of Dubai.

Health Regulation Sector

Dubai Health Authority

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INTRODUCTION

The Health Regulation Sector (HRS) plays a key role in regulating the health sector. HRS is mandated by the Dubai Health Authority (DHA) Law No. (6) of the year (2018) with its amendments pertaining to DHA, to undertake several functions including but not limited to:

- Developing regulation, policy, standards, guidelines to improve quality and patient safety and promote the growth and development of the health sector;
- Licensure and inspection of health facilities as well as healthcare professionals and ensuring compliance to best practice;
- Managing patient complaints and assuring patient and physician rights are upheld;
- Governing the use of narcotics, controlled and semi-controlled medications;
- Strengthening health tourism and assuring ongoing growth; and
- Assuring management of health informatics, e-health and promoting innovation.

The Standards for Stem Cells and Regenerative Medicine aims to fulfill the following overarching Dubai Health Sector Strategy 2026:

- Pioneering Human-centered health system to promote trust, safety, quality and care for patients and their families.
- Make Dubai a lighthouse for healthcare governance, integration and regulation.
- Leading global efforts to combat epidemics and infectious diseases and prepare for disasters.
- Pioneering prevention efforts against non-communicable diseases.
- Become a global digital health hub.

- Foster healthcare education, research and innovation.
- Strengthening the economic contribution of the health sector, including health tourism to support Dubai economy.

EXECUTIVE SUMMARY

The purpose of this standard is to provide a structured regulatory framework that aligns with international best practices and national regulations. These standards outline the essential standards for stem cell and regenerative medicine practices, ensuring compliance with regulatory and ethical frameworks. It provides structured requirements on governance, donor selection, laboratory infrastructure, quality management, clinical applications, and ethical considerations. By integrating international best practices, these standards aim to enhance patient safety, product efficacy, and regulatory compliance. Key highlights include:

- Governance and institutional oversight
- Accreditation and quality assurance requirements
- Donor eligibility and informed consent protocols
- Stem cell collection, processing, cryopreservation, and storage
- Ethical and legal considerations
- Strategic collaborations and research

This framework ensures that stem cell practices operate with the highest levels of ethical conduct, regulatory compliance, and quality assurance, thereby safeguarding patient safety and promoting continuous improvement in clinical outcomes.

DEFINITIONS

AABB (Association for the Advancement of Blood & Biotherapies) is An organization that establishes standards for blood banking, transfusion medicine, and cellular therapy.

Adverse event: any unintended or unfavourable symptom or condition that is temporary and associated with an intervention that may have a causal relationship with the intervention, medical treatment, or procedure

Accreditation is an official recognition that an institution meets predefined quality and safety standards in stem cell therapy and regenerative medicine.

Autologous Transplantation is a procedure in which a patient's healthy stem cells (bloodforming cells) are collected from the blood or bone marrow before treatment, stored, and then given back to the patient after treatment. An autologous stem cell transplant replaces a patient's stem cells that were destroyed by treatment with radiation or high doses of chemotherapy. An autologous stem cell transplant is most often used to treat blood cancers, such as myeloma, leukaemia and lymphoma.

Allogeneic Transplantation is a procedure in which a patient receives healthy bloodforming cells (stem cells) from a donor to replace their own stem cells that have been destroyed by treatment with radiation or high doses of chemotherapy. In an allogeneic stem cell transplant, the healthy stem cells may come from the blood or bone marrow of a related donor who is not an identical twin of the patient or from an unrelated donor who is genetically similar to the patient. An allogeneic stem cell transplant is most often used to treat blood cancers, such as leukemia and lymphoma, and certain types of blood or immune system disorders.

Biosafety Cabinet (BSC) is A containment device used to handle stem cell cultures under controlled conditions, minimizing contamination risks.

Clinical Program: an integrated medical team housed in a defined location. The program includes a Clinical Program Director who can demonstrate sufficient staff training, adoption of protocols, written Standard Operating Procedures, implementation of quality management systems, clinical outcome analysis, and regular interaction among clinical sites

Corrective and Preventive Actions (CAPA) are Procedures used to investigate and correct quality deviations and prevent recurrence.

Cryopreservation is The process of preserving cells or tissues at extremely low temperatures to maintain viability.

Differentiation is The process by which stem cells develop into specific cell types with specialized functions.

Donor Eligibility Assessment is A set of medical, laboratory, and risk criteria to determine the suitability of a donor for stem cell collection.

Exosomes are Extracellular vesicles secreted by stem cells that mediate intercellular communication.

Ethics Committee (EC)/Institutional Review Board (IRB) is A regulatory body responsible for reviewing and approving ethical aspects of research involving human participants.

Environmental Monitoring are Continuous assessment of laboratory conditions such as temperature, humidity, and contamination levels.

FACT (Foundation for the Accreditation of Cellular Therapy) is An international organization that sets standards for cellular therapies and regenerative medicine.

Good Manufacturing Practices (GMP) is A system ensuring products are consistently produced and controlled according to quality standards.

Graft-versus-Host Disease (GVHD) is A condition in which immune cells from a donor attack the recipient's tissues after transplantation.

Hematopoietic Stem Cells (HSCs) are Stem cells that give rise to blood and immune system cells.

Induced Pluripotent Stem Cells (iPSCs) are Reprogrammed adult cells that behave like embryonic stem cells.

Informed Consent: refers to an agreement or permission accompanied by full information on the nature, risks, and alternatives of a surgical or interventional procedure before the physician begins the procedure/treatment. Accordingly, the patient either consents to or refuses treatment.

Institutional Review Board (IRB) is A body that ensures research involving human participants adheres to ethical and legal standards.

Mesenchymal Stem Cells (MSCs) are Multipotent stromal cells capable of differentiating into bone, cartilage, and fat cells.

Quality Management Program (QMP) is A structured system that ensures quality control and continuous improvement in stem cell processing and application.

Regenerative Medicine is A branch of medicine focused on replacing, repairing, or regenerating damaged tissues or organs using stem cells.

Stem Cells are Undifferentiated cells with the potential to develop into various specialized cell types.

Standard Operating Procedures (SOPs) are Written instructions detailing standardized methods for stem cell collection, processing, storage, and transplantation.

Traceability is defined as the ability to track stem cell products from donor to recipient to ensure safety and regulatory compliance.

ABBREVIATIONS

AABB	:	Association for the Advancement of Blood & Biotherapies
BSC	:	Biosafety Cabinet
CAP	:	College of American Pathologists
CAPA	:	Corrective and Preventive Actions
CFR	:	Code of Federal Regulations
DHA	:	Dubai Health Authority
EC	:	Ethics Committee
EMA	:	European Medicines Agency
FACT	:	Foundation for the Accreditation of Cellular Therapy
FDA	:	Food and Drug Administration
GMP	:	Good Manufacturing Practices
GVHD	:	Graft-versus-Host Disease
HSC	:	Hematopoietic Stem Cells
iPSC	:	Induced Pluripotent Stem Cells
IRB	:	Institutional Review Board
ISBT	:	International Society of Blood Transfusion
ISO	:	International Organization for Standardization
LN2	:	Liquid Nitrogen
MSC	:	Mesenchymal Stem Cells
QMP	:	Quality Management Program

QMS	:	Quality Management System
SOP	:	Standard Operating Procedure
WHO	:	World Health Organization

1. BACKGROUND

Stem cells and regenerative medicine have emerged as transformative fields in modern healthcare, offering innovative solutions for various medical conditions, including genetic disorders, degenerative diseases, and tissue regeneration.

Stem cell-based therapies and regenerative medicine have shown significant potential in treating chronic and life-threatening conditions. The increasing global interest in these therapies necessitates a structured regulatory approach to ensure patient safety and treatment efficacy. These standards encompass governance, ethical considerations, laboratory infrastructure, accreditation, donor eligibility, and clinical applications, ensuring compliance with globally recognized benchmarks such as FACT, AABB, GMP, and ISO 15189. This document covers both autologous (self-derived) and allogeneic (donor-derived) stem cell applications and includes provisions for ex vivo processing, cryopreservation, and clinical administration.

The primary purpose of these standards is to:

- Ensure the safety, quality, and efficacy of stem cell-based therapies.
- Establish ethical and governance principles for stem cell research and clinical applications.
- Provide accreditation and quality assurance mechanisms for stem cell laboratories.
- Standardize donor eligibility and informed consent protocols.
- Enhance collaboration among regulatory bodies, healthcare institutions, and research organizations.

2. SCOPE

2.1. Stem cells and Regenerative medicine services in DHA licensed health facilities.

3. PURPOSE

3.1. To ensure provision of the highest levels of safety and quality of Stem cells and Regenerative Medicine services in Dubai Health Authority (DHA) licensed health facilities.

4. APPLICABILITY

4.1. These standards apply to all stakeholders involved in stem cell and regenerative medicine, including:

4.1.1. Healthcare professionals handling stem cell therapies

4.1.2. Laboratory personnel processing and storing stem cells

4.1.3. Researchers conducting clinical trials or preclinical studies

4.1.4. Regulatory authorities responsible for compliance and oversight

4.1.5. Ethics committees reviewing and approving stem cell research and treatments

5. **STANDARD ONE:** GOVERNANCE AND INSTITUTIONAL FRAMEWORK

Governance and Oversight for Stem Cell Practices

5.1. Healthcare organizations shall establish a clear governance framework, designating personnel responsible for overseeing stem cell programs.

5.1.1. This includes leadership across medical, scientific, and administrative domains.

5.2. A comprehensive Quality Management Program (QMP) shall be implemented to govern all activities related to stem cell collection, processing, and clinical applications. This program should encompass:

5.2.1. Internal and external audits to ensure compliance.

5.2.2. Corrective and Preventive Actions (CAPA) to address non-compliance or areas for improvement.

5.2.3. Ongoing performance evaluations to guarantee alignment with international standards.

Compliance with Regulatory and Ethical Standards

5.3. All stem cell practices shall comply with local, national, and international regulations, including but not limited to the following:

5.3.1. FDA

5.3.2. EMA

5.3.3. WHO Good Manufacturing Practices (GMP)

5.3.4. FACT-JACIE standards

5.4. Informed consent shall be obtained from both donors and recipients.

5.4.1. All procedures should be conducted in accordance with the ethical principles outlined in Institutional Review Board (IRB) or Ethics Committee approvals.

Collection and Processing Oversight

5.5. All procedures involved in stem cell collection, handling, and processing shall be performed in accordance with documented SOPs.

5.5.1. These SOPs should be regularly reviewed and updated to maintain compliance with the latest standards.

5.6. Procedures shall only be performed by professionals who have received proper training and certification.

5.6.1. The competence of personnel shall be assessed regularly through documented competency evaluations, with continuous education programs.

5.7. Stem cell processing and storage shall occur in controlled environments that adhere to GMP or equivalent standards, ensuring product quality and safety.

Quality Assurance and Monitoring

5.8. Regular internal and external audits shall be conducted to assess the organization's adherence to relevant regulations and standards.

5.9. A formal system shall be in place for reporting, investigating, and resolving adverse events or non-conformances related to stem cell practices.

5.10. For Data Management and documentation ensure the following:

5.10.1. Complete traceability of cellular products from donor to recipient is required to ensure full accountability.

5.10.2. All procedures, test results, and associated documentation shall be accurately recorded and securely maintained in accordance with data integrity standards.

5.10.3. Clinical outcomes shall be continuously monitored to assess the safety and efficacy of therapies.

Accreditation and Continuous Improvement

5.11. Stem cell programs shall achieve and maintain accreditation from reputable organizations, including FACT, GMP, AABB, and other internationally recognized accrediting bodies, ensuring adherence to the highest standards of practice.

5.12. Personnel shall engage in ongoing training and professional development programs to stay informed about advancements in the field.

5.12.1. Documented competency assessments shall be conducted regularly to ensure up-to-date knowledge and skill levels.

Ethical and Operational Transparency

5.13. All stem cell-related research and clinical practices shall undergo review and approval by an Institutional Review Board (IRB) or Ethics Committee to ensure ethical standards are upheld.

5.14. Clear and transparent communication with patients, donors, and other relevant stakeholders is mandatory. This communication shall provide comprehensive information regarding the risks, benefits, and available alternatives to the proposed treatments.

6. **STANDARD TWO**: FACILITIES AND INFRASTRUCTURE

6.1. Facilities involved in stem cell practices in Dubai shall adhere to stringent design, construction, and operational safety standards to ensure the highest level of quality and safety in cellular therapy.

6.2. All facilities shall adhere to cleanroom classifications stated in **appendix 1.**

6.3. Health facilities with stem cells and regenerative medicine services shall have environmental Control and Monitoring:

6.3.1. Real-time monitoring of temperature, humidity, and airborne particle counts is mandatory.

6.3.2. Temperature Stability: Laboratory areas shall maintain a temperature range of 18-22°C, with humidity levels below 60% RH to prevent moisture build-up.

6.3.3. HEPA Filtration: HEPA filters with 99.97% efficiency (0.3µm) are required, with automated alarms to detect deviations from acceptable levels.

6.3.4. Backup Systems: Critical storage areas shall be supported by redundant power supplies, monitored 24/7, with emergency protocols in place for temperature excursions beyond ±2°C.

6.4. Autologous and Allogeneic Workflow should be separated:

6.4.1. Autologous (patient-specific) and allogeneic (donor-derived) product handling shall be physically segregated.

6.4.2. Color-coded Zoning:

a. Blue zones for autologous processing

b. Green zones for allogeneic processing

c. Red zones for hazardous waste handling

6.4.3. Independent air-handling units (AHUs) shall be installed for each zone to ensure separate airflow and minimize contamination.

6.4.4. A defined movement plan shall be implemented to restrict personnel from transitioning between zones without adequate decontamination.

6.4.5. Separate gowning and decontamination areas shall be designated for each zone to prevent cross-contamination.

6.5. A one-way, linear workflow should be established from sample reception to processing to cryostorage, without backtracking or unnecessary personnel movement.

6.6. Pass-through autoclaves and material airlocks are recommended to minimize manual handling and contamination risks.

6.7. Decontamination stations shall be positioned at all exit points to reduce cross-contamination risks.

6.8. Positive pressure differentials shall be maintained in clean zones, with negative pressure areas allocated for waste and biohazard containment.

6.9. All stem cell facilities shall strictly adhere to the established cryogenic storage standards to ensure the long-term viability and integrity of cryopreserved cellular products.

6.9.1. Refer to **appendix 2** for storage and cryopreservation requirements.

6.10. Stem cell facilities shall fully comply with rigorous construction and biosafety requirements to ensure a safe, sterile, and compliant environment for all laboratory activities.

6.10.1. This includes the use of non-porous, chemical-resistant materials for walls and flooring, as well as maintaining strict pressure differentials within cleanroom and hazardous waste areas.

6.10.2. HVAC systems shall be designed with redundancy and humidity control to ensure consistent air quality. Additionally, biosafety cabinets (BSCs) shall be utilized and certified annually, and oxygen monitoring systems shall be in place in cryogenic storage areas to prevent asphyxiation hazards.

6.10.3. Refer to **appendix 3** for construction and biosafety requirements.

6.11. Laboratory personnel shall adhere to mandatory PPE requirements by wearing gowning suits, sterile gloves, shoe covers, and eye protection.

6.11.1. Cooling vests should be provided for staff working in high-temperature environments.

6.12. Staff shall complete quarterly drills on LN2 safety, fire evacuation, and cybersecurity threats.

6.13. Training shall be conducted by accredited institutions recognized by the DHA, WHO, or other international regulatory bodies.

6.14. Stem cell facilities shall adhere to strict equipment selection and calibration standards to ensure accurate, reliable, and compliant operations.

6.14.1. Only centrifuges, incubators, and cryogenic storage units approved by local regulators may be used in laboratory processes.

6.14.2. All equipment shall be equipped with backup redundancy systems to minimize the risk of downtime.

6.14.3. Calibration schedules for critical equipment shall be strictly followed, with pipettes calibrated every 6 months in line with Dubai Municipality Metrology Guidelines, and incubators, freezers, and particle counters calibrated annually to maintain precision and ensure regulatory compliance.

6.15. Stem cell facilities shall comply with firm waste management and sustainability standards to ensure safe and responsible disposal of biohazardous and chemical waste.

6.15.1. Sharps shall be disposed of in labelled, puncture-proof containers, and all waste handling shall be conducted by Dubai Municipality licensed waste contractors.

6.15.2. For chemical waste, formaldehyde and other hazardous materials shall be neutralized or chemically treated before disposal, in full compliance with Dubai Municipality's Hazardous Waste Regulations.

6.15.3. These measures are essential to protect public health and the environment while maintaining regulatory compliance.

7. **STANDARD THREE:** QUALITY MANAGEMENT SYSTEM

7.1. A compliant Quality Management System (QMS) shall adhere to the following principles to ensure quality and compliance in stem cell processing and regenerative medicine:

7.1.1. Prioritize patient and donor safety and minimize risks in all processes involving stem cell administration and processing.

7.1.2. Ensure full compliance with national and international regulations governing cellular therapies.

7.1.3. Implement risk identification, analysis, and mitigation strategies, documenting all actions.

7.1.4. Establish mechanisms for ongoing quality improvements and regulatory compliance monitoring.

7.1.5. Maintain complete and secure documentation, data protection, and audit trails to ensure traceability and accountability.

7.2. A clear and structured organizational hierarchy is essential for ensuring QMS compliance and maintaining high operational standards.

7.2.1. Each facility shall define roles and responsibilities for managing quality policies, processes, and regulatory adherence.

7.3. Facilities shall appoint a qualified Quality Manager with independent authority to oversee and ensure compliance with the QMS.

7.3.1. The Quality Manager is responsible for conducting internal audits, managing deviations, and facilitating continuous improvement.

7.4. Senior management, including the Laboratory Director and key executives, shall allocate necessary resources, define quality objectives, and ensure alignment with regulatory standards.

7.4.1. They are also responsible for fostering a culture of quality, accountability, and transparency within the organization.

7.5. Facilities shall conduct quarterly management reviews to assess quality performance, KPIs, and implement corrective and preventive actions (CAPA). The review process should include:

7.5.1. Evaluation of quality objectives to align with organizational goals.

7.5.2. Assessment of audit findings and regulatory compliance.

7.5.3. Analysis of nonconformities and CAPA effectiveness.

7.5.4. Review of resource and training requirements for operational efficiency.

7.5.5. Stakeholder feedback assessment to optimize services and processes.

7.6. Each facility shall maintain a documented Quality Policy Statement that:

7.6.1. Defines the facility's commitment to patient safety, product quality, and regulatory compliance.

7.6.2. Establishes measurable objectives for continuous quality improvement and process optimization.

7.6.3. Ensures alignment with international and local regulatory standards.

7.6.4. Is accessible to all employees and stakeholders, fostering awareness and compliance.

7.7. All personnel shall undergo mandatory initial and recurring training tailored to their roles, including theoretical knowledge, hands-on practice, and regulatory compliance.

7.8. Competency assessments shall be conducted at defined intervals, with non-compliance resulting in suspension from critical operations. Training records shall be securely maintained and available for audits.

7.9. Standard Operating Procedures (SOPs) shall be developed and maintained for all critical processes, with regular reviews and updates.

7.9.1. Both electronic and paper records shall be securely maintained with controlled access, and retained for a minimum of 10 years.

7.10. Quality Assurance (QA)

7.10.1. The QA program shall oversee internal audits, nonconformance handling, and corrective actions. QA ensures that laboratory procedures comply with regulatory and accreditation standards.

7.10.2. All QA processes, including verification of SOP adherence, shall be documented. Laboratories shall participate in external proficiency testing programs to validate test accuracy.

7.10.3. Facilities should establish a structured program to collect feedback from healthcare providers, patients, and regulatory authorities.

7.10.4. Facilities shall Conduct an Annual Quality Review to evaluate the effectiveness of improvements and document progress towards quality objectives. Corrective action plans shall be tracked and implemented.

7.11. All laboratory processes shall conform to internationally recognized standards, including:

7.11.1. FACT-JACIE International Standards for Cellular Therapy

7.11.2. AABB Standards for Cellular Therapy Services

7.11.3. WHO GMP Guidelines for Blood Establishments

7.11.4. ISO 15189: Medical Laboratories – Requirements for Quality and Competence

7.11.5. European Medicines Agency (EMA) Standard for regenerative medicine.

8. **STANDARD FOUR:** DONOR ELIGIBILITY, RECRUITMENT, AND CONSENT

8.1. All donors shall undergo a comprehensive screening process, including a review of medical history, laboratory testing, physical examination, and risk assessment, to ensure the safety of both donor and recipient. Screening shall be conducted by a qualified medical professional and documented accordingly.

8.2. Allogeneic donors shall be tested for transfusion-transmissible infections (TTIs), including but not limited to:

8.2.1. HIV-1, HIV-2 (serology and nucleic acid testing)

8.2.2. Hepatitis B (HBsAg, HBV DNA, and anti-HBc)

8.2.3. Hepatitis C (HCV RNA and anti-HCV)

8.2.4. Syphilis (Treponema pallidum testing)

8.2.5. HTLV-I/II (where required by law)

8.2.6. CMV (for certain recipient populations requiring CMV-negative donors)

8.2.7. Additional screening for West Nile Virus, Zika Virus, and SARS-CoV-2 based on regional prevalence and regulatory guidance.

8.3. Eligibility criteria for cellular therapy products vary based on donor characteristics, sample source, and intended use.

8.3.1. Each sample type has specific screening, collection, and quality control requirements to ensure safety and compliance with international standard.

8.4. The eligibility for various cellular therapy products requires adherence to specific criteria based on the source of the cells and donor health.

8.5. Donors for Hematopoietic Progenitor Cells (HPCs), Mesenchymal Stem/Stromal Cells (MSCs), Adipose-Derived Stem Cells (ADSCs), Stromal Vascular Fraction (SVF), and Induced Pluripotent Stem Cells (iPSCs) shall meet age, health screening, and genetic compatibility requirements.

8.5.1. All donors shall be screened for infectious diseases, cancer, blood disorders, and other health conditions to ensure the safety of both the donor and the recipient.

8.5.2. Ethical considerations guide both allogeneic and autologous donations, ensuring voluntary, informed consent, and long-term monitoring for potential risks.

8.5.3. Compliance with these eligibility requirements in appendix 4 is essential to maintain safety, efficacy, and regulatory standards.

8.6. Implications for Future Treatment Options:

8.6.1. Allogeneic Donations:

a. Risk of graft-versus-host disease (GVHD) necessitates careful donor selection and immune compatibility testing.

b. Advances in gene-editing technologies and immune modulation may enhance allogeneic therapies.

8.6.2. Autologous Donations:

a. Potential for future therapies if cells are stored properly.

b. Personalized cell-based treatments, including gene therapy and regenerative medicine, could benefit from the use of the patient's own cells.

8.7. Ethical Considerations in Recruitment

8.7.1. Donor recruitment shall be transparent, ethical, and non-coercive.

8.7.2. Potential donors shall receive comprehensive information regarding the donation process, risks, and future use of their cells.

8.7.3. Marketing materials shall comply with regulatory standard and be factual and clear.

8.8. Donor Education and Counselling

8.8.1. Educational materials shall be culturally appropriate and scientifically accurate, including:

a. Purpose and scope of donation.

b. Short-term and long-term health risks.

c. Alternative treatment options for recipients.

d. Possibility of commercialization of donated material.

8.8.2. Qualified healthcare professionals shall be available to address donor concerns.

8.9. Informed Consent Process

8.9.1. Written informed consent shall be obtained before any medical screening.

8.9.2. The consent process should include:

a. Detailed explanation of risks and benefits.

b. The right to withdraw consent at any time.

c. Confidentiality and data protection.

d. Information on potential research or therapeutic applications.

8.9.3. Consent forms shall be standardized, validated, and approved by an ethical review board.

9. **STANDARD FIVE:** COLLECTION, PROCESSING, CRYOPRESERVATION, AND STORAGE

9.1. Allogeneic stem cells are derived from a genetically different individual, often a donor.

9.1.1. The collection of these stem cells is vital for life-saving treatments such as hematopoietic stem cell transplantation (HSCT), regenerative medicine, and research.

9.1.2. Given that these stem cells are genetically distinct from the recipient, the process is fraught with challenges and risks, including immune rejection and potential disease transmission.

9.2. Donors shall undergo comprehensive medical assessments, including a review of their medical history, physical examination, and laboratory testing for infectious diseases (HIV, Hepatitis B & C, Syphilis, etc.).

9.2.1. HLA typing and genetic screening are required to confirm donor-recipient compatibility and prevent immune rejection.

9.2.2. The screening should also check for hereditary conditions that could impact the safety and efficacy of the stem cells.

9.2.3. Long-term follow-ups to assess the donor's health are required, ensuring compliance with DHA regulations on donor health and safety.

9.3. Donor recruitment efforts shall align with DHA's ethical standard, ensuring that the process is voluntary, transparent, and free from coercion.

9.3.1. The recruitment strategy shall prioritize transparency and provide clear information about the process and potential risks.

9.3.2. The recruitment should focus on encouraging a diverse donor pool, improving the potential for suitable matches for patients, and enhancing the availability of stem cells for a wide range of therapeutic applications.

9.3.3. All donors shall be fully informed about the collection process, storage, potential uses, and associated risks.

9.3.4. Donors shall sign consent forms voluntarily, understanding the implications of their participation.

9.3.5. Consent forms shall be securely stored as per DHA's documentation requirements, ensuring traceability during audits and future compliance checks.

9.4. DHA outlines clear standard for donor deferral based on temporary conditions (such as recent infections) and permanent conditions (e.g., chronic illness).

9.4.1. If ineligible, donors shall be informed of the reasons and provided guidance on future eligibility.

9.5. The rationale for any deferral decision shall be documented and monitored, ensuring compliance with DHA standards and regulations.

9.6. See appendix 5 for Stem cell Collection Methods by Source.

9.7. Comprehensive patient evaluations, including medical history reviews, imaging studies, and laboratory tests, shall be completed to assess the patient's suitability for stem cell collection

9.7.1. Including any risk factors (e.g., clotting disorders, metabolic issues) should be identified and managed before collection in compliance with DHA standards.

9.8. Patient Recruitment practices shall ensure that patients fully understand the procedure, benefits, and risks involved. Ethical practices aligned with DHA standard shall be followed to prevent coercion.

9.9. The health facility shall ensure a thorough Consent Process and Documentation

9.9.1. The consent process shall be clear and thorough, covering the collection methods, risks, storage conditions, and future therapeutic uses.

9.9.2. DHA requires written consent from patients after they have acknowledged full understanding of the procedure.

9.10. Patient Deferral decisions shall adhere to DHA's medical standard, ensuring the safety and quality of autologous stem cells.

9.10.1. All deferral decisions should be communicated clearly to patients, with complete documentation maintained for compliance.

10. STANDARD SIX: PRODUCT TESTING, VALIDATION, AND QUALITY ASSURANCE

10.1. Product testing is a systematic process to assess regenerative medicine products to meet predefined specifications and regulatory requirements.

10.1.1. This process includes physical, chemical, biological, and functional evaluations.

10.2. Cell Identity testing:

10.2.1. Short Tandem Repeat (STR) Analysis: STR analysis shall be performed to determine the cell line identity.

a. For autologous cell therapy, STR shall match 100% between donor and recipient; otherwise, the cell line is considered non-autologous.

10.2.2. Flow cytometry is used to identify corresponding cell markers to determine cell type.

a. For mesenchymal stem cells, CD73, CD90, and CD105 are positive markers, while CD34, CD45, and HLA-DR are absent.

10.3. Cell Purity testing

10.3.1. Flow Cytometry Analysis should be Used to determine the percentage of the desired cell population.

a. MSCs shall be >95% positive for CD73, CD90, and CD105, with <2% cells positive for CD34, CD45, and <1% for HLA-DR.

10.3.2. Pathogen Testing to assess Cell lines and primary cells are free from human pathogenic viruses, including hepatitis virus (HCV, HBV, HAV), HIV-1/2, HHV, HPV, and HTLV-1/2.

10.3.3. Sterility Testing shall be Performed after cell isolation, prior to cryopreservation, and before transplantation to ensure absence of bacterial, mycoplasma, and fungal contamination.

10.4. Stem Cell Potency testing

10.4.1. Morphological Observation to assess stem cells' characteristics visually, including size, shape, and colony structure.

10.4.2. Marker Analysis (Immunocytochemistry, Flow Cytometry, RT-PCR): Identifies surface markers or transcription factors associated with stem cell potency.

a. Pluripotent stem cells express OCT4, SOX2, NANOG, and TRA-1-60, TRA-1-81, SSEA-4.

10.5. Cell Viability testing

10.5.1. Dye Exclusion Tests (e.g., Trypan Blue or 7-AAD dye via flow cytometry): Live cells remain unstained, while dead cells turn blue.

10.5.2. Metabolic Activity Assays (e.g., MTT Assay, Alamar Blue Assay): Determines cell viability based on metabolism, with ATP-based methods preferred for accurate quantification.

10.6. Genetic Stability testing

10.6.1. Cytogenetics Testing (Karyotyping / FISH): Detects ploidy level of cells.

10.6.2. Tumorigenic Mutation Analysis: Conducted during master cell banking to evaluate potential mutations.

10.6.3. Whole Genome Sequencing / Whole Exome Sequencing: Detects gene mutations or genetic variations.

10.7. Cell Safety Release for Transplantation testing

10.7.1. Tumorigenicity Testing: Ensures the absence of remaining pluripotent stem cells, mitigating the risk of tumor formation. Methods include PCR for pluripotency markers (e.g., Oct3/4).

10.7.2. Abnormal Differentiation Risk Assessment: Evaluates stem cells for lineage commitment stability before clinical application.

10.8. Preclinical Studies include the following:

10.8.1. In Vitro Studies:

a. Artificial Intelligence and In Silico Design: Supports optimization of experimental strategies.

b. Cell and Cell-Derived Product Testing: Includes testing for cytokines, peptides, proteins, hormones, exosomes, and extracellular vesicles.

c. 3R Principle (Replace, Reduce, Refine): Encourages the use of animal-free in vitro models such as organoid engineering and organ-on-a-chip models.

10.8.2. In Vivo Studies

a. Animal Models: Common species include mice, rats, rabbits, and pigs, with in vitro analysis preceding animal studies.

b. Compliance with International Animal Welfare Standard: The 3R principle (Replace, Reduce, Refine) shall be applied.

10.8.3. Validation

a. Validation ensures that processes and methods used during product development consistently produce results that meet defined standards.

b. Installation Qualification (IQ): Verifies proper installation of equipment and facilities.

c. Operational Qualification (OQ): Ensures equipment operates per specifications, ensuring GMP compliance.

d. Performance Qualification (PQ): Assesses the entire process under simulated production conditions.

10.9. Assay Validation Ensures that analytical methods are accurate, reliable, and reproducible.

10.9.1. This includes Validation Parameters:

a. Specificity: Ability to measure the intended analyte without interference.

b. Accuracy: Agreement between measured values and absolute standards.

c. Precision: Reproducibility of results across independent biological replications.

d. Linearity: Assay shall show proportional results to analyte concentration ($r > 0.95$).

e. Sensitivity: Defines the lowest detectable level of the analyte.

f. Independence: Each data point shall be independent to avoid pseudo-replication.

10.10. Role of Quality Assurance (QA) in Regenerative Medicine

10.10.1. Establishment and maintenance of Standard Operating Procedures (SOPs).

10.10.2. Ongoing training and monitoring of laboratory personnel.

10.10.3. Oversight of cell and cell-derivative production processes to prevent errors.

10.11. Good Manufacturing Practices (GMP) Includes controlled laboratory environments to prevent contamination, traceability of materials and processes, and documentation of all manufacturing activities.

10.12. Ensure the use of Batch Manufacturing Records (BMRs) to document all cell isolation, expansion, cryopreservation, storage conditions, and product derivation.

11. **STANDARD SEVEN:** CLINICAL APPLICATION AND ADMINISTRATION

11.1. Stem cell therapy is used in regenerative medicine, tissue restoration, and disease modification has been extensively studied and continues to undergo clinical trials.

11.1.1. Stem cells possess the unique ability to transform into multiple cell and tissue types, making them suitable for numerous therapeutic applications.

11.2. Therapeutic Applications include:

11.2.1. Hematopoietic Stem Cell Transplantation (HSCT): Used for hematological malignancies, bone marrow failure syndromes, and genetic disorders such as thalassemia and sickle cell disease.

11.2.2. Mesenchymal Stem Cells (MSC): Applied in autoimmune diseases (e.g., graft-versus-host disease), orthopedic injuries, and inflammatory conditions.

11.2.3. Neural Stem Cells (NSC): Used for treating neurodegenerative disorders such as Parkinson's disease, spinal cord injuries, and stroke rehabilitation.

11.2.4. Cardiac Stem Cells: Applied in myocardial infarction and chronic heart failure management.

11.2.5. Exosomes: Investigational use in regenerative medicine, including wound healing, anti-inflammatory therapies, and neuroprotection.

11.3. Investigational Applications include:

11.3.1. Induced Pluripotent Stem Cells (iPSCs): Used for disease modelling, drug testing, and personalized regenerative therapies.

11.3.2. Embryonic Stem Cells (ESC): Restricted to ethically approved research settings for studying developmental biology and exploring potential therapeutic uses.

11.4. Not all patients are suitable candidates for stem cell therapy. Eligibility is determined by factors such as the disease type, the condition's stage, the patient's overall health, and the stem cell type used.

11.5. Acute vs. Chronic Conditions: Stem cell therapy is often more effective in the early stages or acute phases of diseases. For example, prompt treatment for neurological conditions like stroke or spinal cord injury may yield better results, while long-term conditions with significant tissue damage may respond less effectively.

11.6. End-Stage Diseases: In cases of end-stage organ failure or advanced degenerative diseases, stem cell regeneration may offer limited benefits, but ongoing progress provides optimism for organ regeneration or disease modification.

11.7. Age and General Health

11.7.1. Age: There is no specific age limit for stem cell therapy, but elderly patients may face reduced regenerative potential due to aging tissues and immune function. Age may be particularly significant in treatments like hematopoietic stem cell transplantation or tissue regeneration.

11.7.2. Comorbidities: Patients with significant comorbid conditions (e.g., uncontrolled diabetes, heart disease) may not be ideal candidates, as these conditions can affect the therapy's success or result in complications.

11.8. Immunological Considerations

11.8.1. Immune System Status: In autologous stem cell treatments (using the patient's own cells), immune compatibility is not a concern. However, in

allogeneic treatments (using donor cells), immune rejection may occur, and the patient may require immunosuppressive therapy.

11.9. Availability of Stem Cells

11.9.1. Source of Stem Cells: The availability of stem cells also influences eligibility. Autologous stem cells are preferred when immune rejection is a risk, but in some cases, allogeneic stem cells may be the only option, raising concerns about tissue compatibility and accessibility.

11.10. Ethical and Legal Considerations

11.10.1. Regulatory Approval: Many stem cell treatments are still experimental and may not be approved by regulatory agencies such as the U.S. FDA or the European Medicines Agency (EMA). Eligibility may depend on whether the treatment is part of a clinical trial or has been approved for broader use.

11.10.2. Ethical Considerations: Ethical concerns, especially regarding the use of embryonic stem cells, may affect patient eligibility, depending on local regulations and institutional policies.

11.11. Risks and Challenges

Despite the potential of stem cell therapies, several risks and challenges persist:

11.11.1. Immune Rejection: A risk in allogeneic stem cell transplants.

11.11.2. Tumorigenicity: Pluripotent stem cells, in particular, may occasionally lead to tumour formation, posing a risk in long-term treatments.

11.11.3. Infection and Complications: The collection, processing, and transplantation methods could introduce infections or cause other complications.

11.11.4. Ethical and Legal Obstacles: The use of embryonic stem cells remains a contentious issue, limiting their application in some regions.

11.12. Administration Protocols

The administration of stem cells requires a well-defined protocol to ensure safety and efficacy. This protocol involves patient selection, stem cell sourcing, processing, preparation, and delivery, along with pre-treatment assessments, post-treatment monitoring, and follow-up care. The specific method of administration varies depending on the type of stem cell and the disease being treated.

11.13. Standardized Administration Methods

Valid protocols are developed to ensure the safety and efficacy of stem cell products and exosomes:

11.13.1. Intravenous (IV) Infusion: Used for systemic administration of hematopoietic stem cells and MSCs.

11.13.2. Intra-articular Injection: Common for orthopedic applications and cartilage repair involving MSCs.

11.13.3. Intrathecal Administration: For treating spinal cord injuries and neurological conditions using NSCs or exosomes.

11.13.4. Intramyocardial Injection: Used for direct cardiac restoration with cardiac stem cells or MSCs.

11.14. Dosage and Preparation

11.14.1. Cell Dosage: Dosage ranges should be standardized based on clinical evidence. For example, 1–5 million cells/kg body weight may be recommended for MSCs in systemic administration.

11.14.2. Preparation: Stem cell products should be prepared in GMP/ISO-certified cleanrooms to meet all quality control standards. Viability testing should confirm a minimum threshold (e.g., >70%), and sterility and endotoxin testing shall be completed before administration.

11.15. Procedure Protocols

11.15.1. Pre-administration: Protocols should include patient preparation, informed consent, and baseline assessments.

11.15.2. Administration: Protocols should detail infusion/injection techniques, monitoring procedures, and equipment requirements.

11.15.3. Post-administration: Monitoring for immediate adverse events and provision of supportive care should be part of the post-administration protocols.

11.16. Real-time Adverse Event Reporting

11.16.1. Systems shall be established for the immediate reporting of adverse events, integrated with national registries as per FACT and AABB standards. Categories of adverse events (e.g., infusion-related reactions, infections, graft failure) should be defined, and standardized reporting formats shall be implemented.

11.17. Root Cause Analysis and Feedback

11.17.1. Adverse events should be investigated through root cause analysis to identify systemic or procedural issues. Monitoring data should be used to update administration protocols and improve patient safety.

12. STANDARD EIGHT: ETHICAL AND LEGAL CONSIDERATIONS

12.1. Stem cell research and regenerative medicine have become pivotal in modern healthcare, offering potential treatments for a variety of diseases, including spinal cord injuries, heart disease, diabetes, neurological disorders, and many other currently untreatable conditions.

12.1.1. Stem cells have the ability to differentiate into various cell types and regenerate tissues, making them a promising avenue for tissue and organ repair. However, the use of stem cells—especially embryonic stem cells—raises significant ethical and legal issues.

12.1.2. These concerns primarily involve the moral status of embryos, consent for cell donation, and potential exploitation or inequitable access to therapies. Additionally, as stem cell research intersects with advancing biotechnologies such as gene editing (e.g., CRISPR), tissue engineering, and 3D bio-printing, new ethical and legal challenges emerge, particularly around altering the human germline or creating genetically modified organisms.

12.2. Ethical Considerations

12.2.1. Source of Stem Cells

a. Embryonic Stem Cells (ESCs): Ethical concerns arise from the destruction of embryos during their collection.

b. Adult Stem Cells: Sourced from bone marrow, adipose tissue, and peripheral blood, these cells require informed donor consent.

c. Induced Pluripotent Stem Cells (iPSCs): Reprogrammed adult cells, which raise concerns about genetic manipulation and potential unintended consequences.

d. Perinatal Stem Cells: Derived from umbilical cord blood and placenta, generally considered ethical with informed parental consent.

12.2.2. Informed Consent

a. Informed consent is a cornerstone of ethical research and clinical practice.

b. Donors and patients shall be fully aware of:

i. The purpose and risks of donating biological materials.

ii. Potential research or commercial uses of the donated biological materials.

12.2.3. Fair Access and Equity

a. Affordability: Ensuring that stem cell therapies are accessible to low-income populations is crucial to avoid exacerbating health inequities.

b. Global Equity: Efforts should address disparities in research priorities, ensuring that underserved or low-income regions also benefit from advancements in regenerative medicine.

12.2.4. Unproven Therapies and Exploitation

a. There are growing concerns regarding unregulated stem cell clinics, such as:

i. Misleading advertising that targets vulnerable patients.

ii. The lack of scientific evidence supporting therapeutic claims.

iii. The absence of long-term safety data for certain stem cell treatments, which may lead to harm if not properly regulated.

12.2.5. Germline Editing, In-Utero Gene Editing, and Human Cloning

a. Germline Editing: Editing human embryos or germline cells for research or therapy is prohibited in many jurisdictions due to ethical concerns about the potential to alter human genetics permanently.

b. In-Utero Gene Editing: Strict ethical reviews are required to prevent prenatal genetic disorders, as any changes could affect future generations.

c. Reproductive Cloning: Reproductive cloning of humans is strictly prohibited due to safety, ethical, and moral concerns regarding the process and its consequences.

12.3. Legal Considerations

12.3.1. International and Regional Legal Landscape

Stem cell research and therapy face varied regulations globally:

a. Permissive Countries: Some countries, such as the UK and Belgium, allow embryonic stem cell research under strict regulations that aim to balance scientific progress and ethical considerations.

b. Restrictive Countries: Countries like Germany and Italy impose strict restrictions on embryonic stem cell research.

c. Islamic Law (UAE): In regions governed by Islamic law, such as the UAE, the destruction and manipulation of human embryos for research and clinical purposes is prohibited.

12.3.2. Research Oversight and Governance

a. Institutional Review Boards (IRBs): These boards ensure that stem cell research complies with ethical and legal standards.

b. Ethics Committees: Provide safeguards for sensitive research involving embryos or human biological materials, ensuring that all activities are ethically sound.

c. Licensing Requirements: Researchers handling human tissues, especially embryos, shall obtain appropriate licenses to ensure compliance with local and international regulations.

12.3.3. Regulation of Clinical Applications

a. Approval Pathways: Regulatory agencies classify stem cell-based products as drugs, biologics, or advanced therapies, and ensure their safety and efficacy before clinical use.

b. Post-Market Surveillance: Regulatory authorities shall continue monitoring the long-term outcomes of stem cell therapies to ensure patient safety.

c. Combating Unproven Therapies: Health authorities (e.g., the Dubai Health Authority) regulate stem cell clinics and educate the public about the risks associated with unproven treatments.

12.3.4. Intellectual Property and Commercialization

a. Patents: While researchers can patent stem cell-derived inventions, ethical concerns remain over "ownership" of human biological materials.

b. Biobanking: Public and private biobanks shall adhere to legal standards regarding the storage, distribution, and use of stem cell lines. These organizations shall maintain transparency and ensure proper consent for use.

12.4. Data Protection in Stem Cell Research

12.4.1. Stem cell research involves collecting and analysing sensitive data, including personal, familial, and genetic information, which necessitates compliance with data protection regulations.

12.5. Compliance with Data Protection Laws

12.5.1. Organizations handling patient data in Dubai shall comply with data protection laws such as:

a. General Data Protection Regulation (GDPR) (Europe).

b. Health Insurance Portability and Accountability Act (HIPAA) (U.S.).

The organization shall ensure full compliance with GDPR or HIPAA when dealing with sensitive biological data.

12.5.2. Patient Anonymity and Data Security

a. Anonymization: It is essential to anonymize donor and patient data in research databases. Publicly sharing identifiable patient information is prohibited.

b. Restricted Access: Only authorized personnel should have access to patient samples and genetic data to protect privacy.

12.5.3. Local Database Regulations

a. Local Storage: Organizations in Dubai shall either maintain a local database or collaborate with approved local data centers to ensure compliance with national regulations.

b. Dubai Health Authority (DHA) Licensing: The DHA oversees the storage of patient data and biological materials. Any organization storing human biological materials for clinical use shall have a GMP-qualified facility and obtain DHA licensing.

c. Research Exemptions: Universities and research institutions that store cells/tissues solely for research purposes, without in vivo use, are exempt from DHA licensing, but shall still obtain necessary approvals from appropriate authorities (e.g., Medical Education departments).

13. STANDARD NINE: STRATEGIC PARTNERSHIPS AND COLLABORATION

13.1. Establishment of Agreements Between Hospitals, Healthcare Centers, and Cord Blood Centers to ensure that all parties comply with internationally recognized quality and safety standards, formal and regularly reviewed agreements are required between hospitals, healthcare centers, and cord blood centers.

13.1.1. These agreements shall align with standards set by FACT, AABB, WHO GMP, and national regulatory standard to ensure product integrity, patient safety, and ethical conduct.

13.2. Regulatory and Compliance Obligations of these agreements include:

13.2.1. Each agreement shall clearly define the scope of responsibilities, including donor screening, collection, testing, processing, storage, distribution, and utilization of cord blood units.

13.2.2. All parties shall comply with national and international accreditation standards and regulatory requirements.

13.2.3. Provisions for periodic regulatory audits and inspections shall be included to ensure ongoing compliance.

13.2.4. Clinical research involving cord blood units shall obtain approval from an Institutional Review Board (IRB) or Ethics Committee before beginning.

13.3. A Standard Operating Procedure (SOP) framework should be integrated into all agreements to standardize the collection, transport, processing, testing, storage, and distribution of cord blood.

13.3.1. All personnel involved in handling cord blood shall undergo initial and periodic competency assessments, in line with accreditation requirements.

13.3.2. Risk mitigation strategies shall be embedded in agreements to address any deviations, nonconformances, or adverse events.

13.4. All agreements shall outline data-sharing protocols that comply with HIPAA, GDPR, and national data protection laws to ensure donor confidentiality and data security.

13.4.1. Electronic tracking systems, such as ISBT 128 labeling and coding, shall be used for maintaining traceability across the supply chain.

13.4.2. Long-term data retention policies should be established to support traceability, regulatory audits, and post-transplant monitoring.

Financial obligations, including cost-sharing for collection, processing, and storage, should be explicitly defined and approved by the Dubai Health Authority (DHA) under the standardized rate framework.

13.4.3. Provisions for liability, indemnification, and dispute resolution should be incorporated into agreements to manage potential legal conflicts.

13.4.4. Research-based collaborations shall clearly outline intellectual property (IP) ownership, ensuring fair distribution of benefits among stakeholders.

13.5. Quality Assurance and Compliance in Collaborative Agreements

All strategic partnerships shall implement a robust quality assurance framework to ensure compliance with Good Manufacturing Practice (GMP), Good Tissue Practice (GTP), and other regulatory requirements.

13.6. All parties in collaboration shall demonstrate compliance with FACT, AABB, CAP, WHO GMP, and relevant national regulatory standard.

13.6.1. Accreditation status of involved parties should be verified and maintained throughout the agreement.

13.6.2. Annual audits shall be performed to verify compliance with quality, safety, and regulatory standards.

13.7. A Corrective and Preventive Actions (CAPA) system shall be implemented to address deviations, adverse events, and nonconformances.

13.7.1. Defined protocols for recall management should be in place in case of product safety issues.

13.7.2. A quarantine system shall be established for cord blood units that fail to meet regulatory and quality criteria.

13.8. Traceability and Chain of Custody Requirements include:

13.8.1. ISBT 128 global standards shall be utilized to ensure complete traceability from collection to transplantation.

13.8.2. Electronic documentation shall capture chain of custody, including time-stamped transfers and storage conditions.

13.8.3. A look-back program shall be in place for retrospective donor risk assessment and post-transplant monitoring.

13.9. Strategic partnerships should support regulated, ethical, and scientifically sound research to advance regenerative medicine and cellular therapies.

13.10. All clinical trials involving cord blood units shall follow approved research protocols and comply with Good Clinical Practice (GCP) standard.

13.10.1. Research studies shall be registered with appropriate regulatory bodies before commencement.

13.10.2. A framework for regulatory oversight should be in place to ensure adherence to ethical and legal standards in collaborative research.

13.11. Ethical Use and Data Governance in Research shall be considered as follows:

13.11.1. Informed consent for research donors shall align with ethical and legal requirements.

13.11.2. Anonymization and de-identification of donor data should be implemented to comply with data protection laws.

13.11.3. Access to shared research data shall be governed by policies to prevent unauthorized usage.

13.12. Strategic partners should engage in ongoing training and competency validation programs to maintain high regulatory and operational standards.

13.12.1. Mandatory training programs should be implemented for all personnel involved in cord blood collection, processing, cryopreservation, and storage.

13.12.2. Nurses and gynecologists involved in collection shall undergo specific training programs, such as those offered by the National Marrow Donor Program (NMDP), to ensure adherence to best practices.

13.12.3. Annual competency assessments shall be conducted for all staff involved in cellular therapy services.

13.12.4. Continuing education programs should provide CME credits to encourage continuous professional development.

13.13. Knowledge Sharing and International Collaboration

13.13.1. Institutions should participate in global conferences and workshops to enhance knowledge and best practices.

13.13.2. International exchange programs should be encouraged to harmonize global standards in stem cell research and transplantation.

13.14. Ethical and Legal Considerations in Strategic Partnerships

All partnerships shall adhere to strict ethical, legal, and compliance frameworks to ensure transparency, donor protection, and public trust.

13.14.1. Ethical Framework for Cord Blood Collection and Utilization

a. Cord blood collection and use shall be voluntary, non-commercial, and ethically justified.

b. Donor recruitment shall follow WHO and national ethical standard to prevent coercion or financial exploitation.

c. Access to stored cord blood shall be equitable, ensuring no commercial bias.

13.15. Regulatory Oversight and Policy Standardization

13.15.1. All stakeholders shall collaborate with national and international regulatory agencies to ensure standardized licensing and operational requirements.

13.15.2. Institutions engaged in cross-border collaborations shall adhere to globally recognized harmonization frameworks.

13.15.3. A compliance monitoring body shall be established to oversee adherence to regulatory and legal provisions.

13.15.4. Reporting, Monitoring, and Continuous Improvement

a. Strategic partnerships shall include continuous performance monitoring and regulatory reporting obligations to ensure compliance and quality improvement.

13.15.5. Regulatory Reporting and Documentation

a. Annual compliance reports shall be submitted to relevant authorities.

b. Risk-based monitoring programs should be implemented to detect deviations from standard operating procedures.

c. Corrective action tracking shall be maintained for all reported nonconformances.

14. STANDARD TEN: ACCREDITATION AND CERTIFICATION

14.1. Laboratories providing stem cell and regenerative medicine services shall comply with FACT-JACIE, AABB, ISO 15189, and other applicable regulatory frameworks mandated by the Dubai Health Authority (DHA).

14.2. Laboratories involved in the manufacturing and processing of cellular therapies shall obtain Good Manufacturing Practice (GMP) certification to meet regulatory and quality standards.

14.3. To ensure the safety, efficacy, and regulatory compliance of products GMP certification is a mandatory requirement, alongside other accreditations such as:

14.3.1. AABB

14.3.2. FACT-JACIE

14.3.3. ISO 15189

14.4. GMP certification shall be acquired from an authorized or accredited regulatory body to ensure adherence to recognized standards.

14.5. Laboratories engaged in the development, clinical application, or commercial distribution of stem cell and regenerative medicine products shall hold GMP certification.

14.6. Laboratories shall develop policies and procedures to ensure the integrity, competency, and traceability of all processes related to stem cell and regenerative medicine services.

14.6.1. Comprehensive records shall be maintained for accreditation assessments, identified nonconformities, and corrective actions to promote continuous improvement.

14.6.2. Regular internal audits and proficiency testing shall be conducted to uphold accreditation and regulatory compliance.

14.6.3. Laboratories shall undergo an initial accreditation assessment, which includes evaluations of:

a. Personnel qualifications
b. Facilities and equipment
c. Testing methodologies
d. Quality Management System (QMS) documentation specific to stem cell processing and regenerative medicine

14.7. Laboratories shall participate in External Quality Assessment Schemes (EQAS) and maintain proficiency testing programs relevant to stem cell and regenerative medicine.

14.8. A continuous improvement process shall be in place, incorporating:

14.8.1. Risk management strategies

14.8.2. Corrective and preventive actions (CAPA)

14.8.3. Periodic management reviews

14.9. Accreditation will be valid for a defined period (e.g., 2-4 years) and is subject to periodic renewal assessments.

14.10. Routine inspections should be conducted annually to ensure ongoing compliance with accreditation and regulatory requirements.

14.11. Laboratories shall submit self-assessment reports and quality performance data as required by the accrediting body for continuous monitoring of compliance.

14.12. Failure to maintain compliance may lead to:

14.12.1. Suspension, probation, or revocation of accreditation

14.12.2. Clearly defined corrective action standard for reinstatement

14.13. Laboratories shall implement internal audit programs to proactively identify nonconformities and carry out corrective actions.

14.14. Laboratories should review emerging industry standards and update accreditation criteria to reflect best practices in stem cell and regenerative medicine.

14.15. All accreditation-related documents, including assessment reports, corrective action plans, and compliance certifications, shall be:

14.15.1. Securely stored

14.15.2. Easily accessible for review by regulatory or accreditation bodies

14.16. Laboratories shall engage in continuous education and training to maintain competencies and stay current with regulatory requirements.

14.17. Collaboration between laboratories, regulatory agencies, and industry stakeholders should be encouraged to:

14.17.1. Harmonize standards

14.17.2. Enhance global accreditation effectiveness

14.18. Noncompliance with accreditation standards will result in:

14.18.1. Documented corrective actions

14.18.2. Defined deadlines for resolution

14.19. Laboratories may appeal accreditation decisions through a structured review process managed by an independent oversight committee within the accrediting body.

14.20. Appeals will be reviewed impartially, with laboratories given the opportunity to present additional evidence supporting their compliance claims.

14.21. Accrediting bodies will maintain and publish a list of accredited laboratories, with regular updates on accreditation status changes, including suspensions and revocations.

15. STANDARD ELEVEN: DATA MANAGEMENT AND REPORTING

15.1. Secure Data Handling Systems

15.1.1. Facilities handling stem cell data shall implement secure digital systems to ensure the confidentiality, integrity, and accessibility of data.

15.2. Data Encryption & Security

15.2.1. All patient and donor data shall be encrypted using Advanced Encryption Standard (AES-256) for both storage and transmission.

15.2.2. Multi-factor authentication (MFA) should be enforced for all data access points to prevent unauthorized access.

15.2.3. Immutable audit logs shall record every access attempt, modification, or deletion of critical data.

15.3. Infrastructure & Compliance

15.3.1. Secure cloud-based storage or on-premise servers should be utilized, ensuring redundancy and disaster recovery mechanisms are in place.

15.3.2. Regular security assessments and penetration testing shall be conducted to identify and resolve vulnerabilities.

15.3.3. Facilities shall comply with GDPR (EU General Data Protection Regulation), HIPAA (Health Insurance Portability and Accountability Act), and ISO 27001 Information Security Management Standards.

15.4. Informed Consent & Patient Rights

15.4.1. Explicit written consent shall be obtained from donors and patients regarding the storage and usage of their data.

15.4.2. Consent forms shall clearly outline how data will be used, shared, anonymized, and protected.

15.5. Anonymization & De-identification

15.5.1. Personally, identifiable information (PII) shall be anonymized or pseudonymized when used for research to protect patient privacy.

15.5.2. Facilities should implement automated data masking techniques to secure sensitive patient information.

15.6. Audit Trails & Access Controls

15.6.1. Role-based access control (RBAC) shall be implemented to limit data access to authorized personnel only.

15.6.2. All data access and modifications shall be logged with detailed timestamps, user identification, and the purpose of access.

15.7. Record keeping Retention Periods

15.7.1. Donor and patient records shall be maintained for a minimum of 10 years after therapy.

15.7.2. Data shall be electronically backed up and stored in at least two geographically separate locations to ensure protection against data loss.

15.8. Metadata & Traceability

15.8.1. Each data entry shall include the date, time, personnel involved, and procedural stage to ensure full traceability.

15.8.2. Electronic Health Record (EHR) systems should incorporate automated quality control checks to minimize manual errors.

15.9. Registry Reporting, Tracking, and Outcome Monitoring

15.9.1. A national registry shall be established to track donor, recipient, and clinical outcomes.

15.9.2. All healthcare institutions are required to report data in real-time, ensuring smooth communication across regions.

15.9.3. Adverse events shall be reported to DHA within 24 hours.

15.9.4. Institutions should utilize standardized reporting templates approved by DHA for uniform data collection.

15.9.5. Predictive analytics should be applied to identify patterns and improve therapeutic protocols.

15.10. Standardized Labelling Protocols

15.10.1. All stem cell products shall have unique ISBT 128-compliant labels, which include:

a. Donation Identification Number (DIN)

b. Product type (e.g., HSC, MSC)

c. Collection and processing dates

d. Storage conditions (e.g., cryopreserved or fresh)

e. Expiration dates

f. Handling instructions

15.10.2. Every label shall include a machine-readable barcode for seamless tracking from collection to transplantation.

15.10.3. Barcodes shall remain legible under cryogenic temperatures.

16. STANDARD TWELVE: RESEARCH AND INNOVATION

16.1. Stem cells and regenerative medicine are at the forefront of modern scientific and medical advancements.

16.1.1. Stem cells possess the unique ability to develop into various specialized cell types, offering the potential to repair or replace damaged tissues and organs.

16.1.2. This has the potential to revolutionize the treatment of a range of conditions such as degenerative diseases, organ failure, injuries, and genetic disorders. However, the research, development, and clinical application of stem cells and regenerative medicine present significant scientific, ethical, and safety challenges.

16.1.3. Issues such as the integrity of stem cell lines, immune rejection, tumour formation, and ethical sourcing of human tissues require careful regulation.

16.2. The Dubai Health Authority (DHA) oversees all research, clinical trials, and commercialization activities related to stem cell therapies and regenerative medicine.

16.2.1. DHA should collaborate with national health agencies, ethics committees, and international bodies to ensure regulatory standards are met.

16.2.2. Only DHA-licensed researchers, scientists, and organizations can conduct preclinical and clinical studies.

16.3. Ethical and Safety Considerations

16.3.1. All research involving human stem cells, including collection, culture, and transplantation, shall adhere to international ethical standards, such as those set by the International Society for Stem Cell Research (ISSCR), FDA, EMA, and local DHA standard.

16.3.2. Sourcing of human stem cells shall respect the autonomy, rights, and dignity of individuals, whether derived from embryos, adult tissues, or induced pluripotent stem cells (iPSCs).

16.3.3. Informed consent shall be obtained from participants providing biological materials for research, ensuring they understand the potential risks and uses of their samples.

16.4. Safety and Risk Assessment

16.4.1. Preclinical safety studies shall be conducted to assess risks such as tumorigenicity, immune rejection, and long-term efficacy.

16.4.2. Stem cell lines shall undergo authentication to prevent contamination and ensure research validity. HLA and STR tests shall be conducted before application in therapy for both autologous and allogeneic cell therapy.

16.4.3. Risk management systems, including monitoring for adverse events during clinical trials, shall be implemented. Sterility tests shall be conducted for biological products.

16.5. Research and Development of Stem Cell Therapies

16.5.1. Entities conducting clinical stem cell research shall obtain a Research License from DHA, which includes protocol review, ethical approvals, and compliance with safety standards.

16.5.2. Each license is valid for a maximum of two years, and new human research or clinical plans require a new license. Extensions can be requested if no changes are made to the original application.

16.6. Clinical Trial Authorization

16.6.1. Clinical trials can only proceed after submitting a Clinical Trial Application (CTA) to DHA, including preclinical data (minimum of 10 independent biological samples), clinical protocols, and ethics committee approval.

16.6.2. DHA mandates that clinical trials include a qualified scientific team, trained technicians, data analysts, responsible hospitals, and a team of physicians.

16.7. Standards for Stem Cell Products

16.7.1. Laboratories manufacturing stem cells or stem cell-based products shall be licensed by DHA, FDA, or EMA based on their current regulations.

16.7.2. Stem cell products shall comply with Good Manufacturing Practices (GMP) to ensure safety, purity, and clinical potency. Only GMP-compliant products are eligible for use in clinical trials.

16.8. Commercialization and Distribution

16.8.1. After successful clinical trials, a Market Authorization application shall be submitted to DHA, including product safety, efficacy, manufacturing practices, and pricing justification.

16.8.2. Selling stem cell therapies below market value is prohibited to avoid market distortion. Pricing shall reflect the full cost calculation, including profit and applicable taxes (e.g., VAT).

16.9. Post-Market Surveillance

16.9.1. Continuous monitoring of stem cell therapies post-commercialization is mandatory to assess long-term safety, effectiveness, and unexpected risks.

16.9.2. Manufacturers are required to report any new side effects or issues to DHA.

16.10. International Collaboration and Innovation

16.10.1. DHA will align national regulations with international standards set by organizations such as ISSCR, WHO, EMA, and FDA.

16.10.2. All stem cell and regenerative medicine research proposals shall receive approval from the Department of Medical Education (MED) before proceeding.

16.10.3. DHA is responsible for providing updated standard for stem cell therapies and regenerative medicine on an annual basis, ensuring that scientists, researchers, and organizations stay informed and comply with the latest standards.

16.11. Compliance, Enforcement, and Penalties

16.11.1. DHA will monitor adherence to regulations through inspections, audits, and clinical trial data reviews. Non-compliance may result in penalties, license suspensions, or legal actions.

16.11.2. Violations may lead to fines, revocation of licenses, or criminal prosecution, depending on the severity of the non-compliance.

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APPENDICES

APPENDIX 1: CLEANROOM CLASSIFICATIONS

Cleanroom Classifications:

1. Grade A cleanrooms (equivalent to ISO Class 5) are designated for high-risk operations requiring stringent contamination control.
    - The maximum allowable airborne particle concentration is 3,520 particles ≥ 0.5 µm per cubic meter, and unidirectional airflow is required to minimize contamination.
    - These cleanrooms are essential for the open processing of cellular products under aseptic conditions.
2. Grade B Cleanroom is suitable for aseptic preparation, filling, and compounding, Grade B cleanrooms maintain ISO Class 5 at rest and ISO Class 7 during operation. Airborne particle limits include:
    - **At rest**: 3,520 particles ≥ 0.5 µm per cubic meter
    - In operation: 352,000 particles ≥ 0.5 µm per cubic meter

      These cleanrooms serve as the buffer zones for Grade A areas to prevent contamination during manufacturing.
3. **Grade C** Cleanroom: Equivalent to ISO Class 7 at rest and ISO Class 8 in operation, Grade C cleanrooms are used for intermediate manufacturing steps. The maximum allowable particle concentration is 352,000 particles ≥ 0.5 µm per cubic meter, ensuring controlled cleanliness during processing.
4. **Grade D** Cleanroom: Grade D cleanrooms are designated for non-aseptic processes and general manufacturing. These spaces are equivalent to ISO Class 8 and allow up to 3,520,000 particles ≥ 0.5 µm per cubic meter. These areas are used for gowning, early-stage manufacturing, and material handling before entering higher-grade cleanrooms.

APPENDIX 2: CRYOPRESERVATION AND STORAGE STANDARDS

1. **LN2 Cryogenic Storage**:
    - Cryogenic storage vessels shall maintain temperatures below −150°C to preserve the viability of cryopreserved cells.
2. **Safe Operating Levels**:
    - **Vapor-phase LN2 storage**: LN2 levels should remain above the minimum fill line, typically ensuring at least 5–10 cm (2–4 inches) of LN2 at the bottom of the vessel.
    - **Liquid-phase LN2 freezers**: LN2 levels should remain above 50% of vessel capacity, with refilling schedules to avoid levels dropping below 30%.
3. **Safety Systems**: Liquid nitrogen storage shall utilize vacuum-insulated tanks with dual temperature probes and continuous data logging for auditing.
4. Automated alarms shall notify staff via SMS or email if:
    - **Temperature fluctuations exceed defined limits.**
    - **LN2 lev**els fall below critical thresholds.
5. **Fire Suppression**: Dubai Civil Defence-approved fire suppression systems shall be installed in all LN2 storage areas.
6. Regular liquid nitrogen replenishment schedules shall be implemented to avoid system failure.
7. Staff handling LN2 shall undergo specialized safety training, including emergency response protocols.
8. **Oxygen Level Monitoring**: Sensors shall be installed in LN2 storage rooms to prevent asphyxiation hazards, and temperature mapping should verify that all areas stay below −150°C.

APPENDIX 3: CONSTRUCTION REQUIREMENTS

1. **Structural Design and Materials - Walls and Flooring**:
    - Use non-porous, chemical-resistant materials (e.g., epoxy resin flooring, stainless steel, reinforced fiberglass wall cladding) to ensure easy cleaning and prevent contamination.
    - Walls shall be seamless and designed for easy disinfection to prevent microbial growth.
    - Anti-static flooring shall be installed in all sensitive areas to prevent electrostatic discharge.
    - Slip-resistant surfaces should be provided in wet zones to ensure personnel safety.
2. **HVAC System and Pressure Mapping**:
    - Pressure **Differentials**: Clean zones shall maintain positive pressure differentials of +15 Pa, while hazardous waste areas shall have negative pressure of -10 Pa.
    - HVAC Redundancy: N+1 redundancy should be implemented in HVAC systems to maintain airflow during equipment failures.
    - Humidity Control: HVAC systems shall incorporate humidity control to prevent excessive moisture accumulation.
    - Routine maintenance and filter replacements for HVAC systems should follow manufacturer recommendations.
3. **Biosafety Protocols - Biosafety Cabinets (BSCs)**:
    - Class II BSCs shall be used for handling stem cell cultures and processing biological samples.
    - BSCs shall be placed away from doorways and high-traffic zones.
    - Annual certification of BSCs shall comply with NSF/ANSI 49 standards.
4. • **Oxygen Monitoring for LN2 Areas**:
    - O2 sensors shall trigger alarms if oxygen levels drop below 18%.

- Sensors should be calibrated monthly using gas mixtures.

5. The **Importance** of ISO/GMP Rooms for Stem Cell Isolation
    - Contamination **Control:** Stem cells are sensitive to contamination, and ISO/GMP rooms are designed to prevent cross-contamination and microbial risks.
    - **Quality and Consistency:** ISO/GMP standards ensure stem cell isolation processes are conducted under controlled conditions, guaranteeing high-quality and consistent products.
    - **Regulatory Compliance:** Stem cell processing shall comply with DHA's regulatory requirements to ensure that products are suitable for clinical use.
    - **Patient Safety:** By minimizing risks during stem cell isolation, ISO/GMP standards protect patients from potential infections or adverse reactions caused by contaminated or substandard products.
    - **Traceability:** Complete traceability is required for all stem cell isolation processes, ensuring that documentation of environmental conditions and procedures is available for audits and compliance.
6. **Cryopreservation** and Storage
    - **Cryopreservation** involves freezing stem cells at very low temperatures to maintain their viability for future use. The process shall be carefully controlled to prevent cell damage due to ice crystal formation. DHA standard for cryopreservation include:
    - **Controlled Freezing:** Use of controlled-rate freezing systems to ensure uniform cooling rates and minimize ice crystal formation

APPENDIX 4: HEMATOPOIETIC PROGENITOR CELLS (HPCS) ELIGIBILITY

1. **Sources**: Bone marrow, peripheral blood (PBSCs), umbilical cord blood (UCB).
2. **Donor Eligibility Criteria**:
    - **Age**:
        - Bone Marrow & PBSC Donors: 18-60 years
        - Umbilical Cord Blood (UCB): Neonatal donors only
    - **Health Screening**:
        - No history of cancer, blood disorders, or autoimmune diseases
        - No chronic infections (HIV, HBV, HCV, syphilis, CMV-active)
        - No high-risk behaviors (IV drug use, travel to malaria-endemic regions)
    - **Genetic & HLA Matching**:
        - Allogeneic donors require HLA compatibility
        - Autologous donors need sufficient stem cell mobilization
    - **Blood Tests**:
        - Hemoglobin ≥ 12.5 g/dL
        - PBSC donors shall respond to G-CSF mobilization
3. **Mesenchymal Stem/Stromal Cells (MSCs) Eligibility**

- **Sources**: Bone marrow, adipose tissue, umbilical cord tissue, amniotic fluid
- **Donor Eligibility Criteria**:
    - **Age**:
        - Bone Marrow MSCs: 18-50 years
        - Adipose MSCs: 18-65 years
        - Umbilical Cord MSCs: Neonatal donors only
        - Amniotic Fluid MSCs: Collected from consenting mothers
    - **Health Screening**:
        - No history of cancer, chronic infections, or inflammatory diseases
        - No recent use of immunosuppressive drugs

- **Tissue Considerations**:
  - Bone marrow MSCs decrease with age; younger donors preferred
  - Adipose MSCs yield higher but can be affected by obesity (BMI >30)
  - Umbilical cord MSCs have high proliferative potential

4. **Adipose-Derived Stem Cells (ADSCs) Eligibility**
   - **Source**: Lipoaspirate or excised adipose tissue
   - **Donor Eligibility Criteria**:
     - **Age**: 18-65 years, with optimal cell yield under 50
     - **Health Screening**:
       - No diabetes, severe obesity (BMI >35), or metabolic syndrome
       - No chronic inflammatory diseases
     - **Tissue Considerations**:
       - Abdominal fat provides higher stem cell yield than thigh/gluteal areas
5. **Stromal Vascular Fraction (SVF) Eligibility**
   - **Source**: Adipose tissue, enzymatically or mechanically dissociated
   - **Donor Eligibility Criteria**:
     - Same health criteria as ADSCs plus:
     - **Infection Risk Assessment**:
       - Screen for contaminants and residual enzymes
       - Ensure sterility for immediate use
     - **Blood Tests**:
       - Normal WBC count (infection-free status)
       - No coagulation disorders to prevent bleeding
     - **Processing Considerations**:
       - Avoid donors with excessive scarring

6. **Induced Pluripotent Stem Cells (iPSCs) Eligibility**
   - **Source**: Somatic cells (skin fibroblasts, peripheral blood mononuclear cells)

- **Donor Eligibility Criteria**:
  - **Age**: 18-55 years (younger cells reprogram better)
  - **Health Screening**:
    - No history of cancer, neurodegenerative diseases, or genetic disorders
    - No chronic viral infections (HIV, HBV, HCV)
  - **Genetic & Epigenetic Factors**:
    - DNA shall be mutation-free for proper reprogramming
    - Avoid donors with high exposure to smoking, radiation, or chronic stress
  - **Storage Considerations**:
    - Requires genetic validation before use
    - Long-term cryopreservation in liquid nitrogen

7. **Allogeneic vs. Autologous Donations**

   The selection of allogeneic versus autologous donations depends on clinical needs, donor availability, ethical considerations, and long-term treatment implications.

- **Ethical Considerations**:
  - **Allogeneic Donations**:
    - Sourced from voluntary, non-remunerated donors to prevent undue influence.
    - Donor rights and well-being shall be safeguarded through independent evaluations and informed consent.
    - Special standard for minors and older donors shall be followed.
  - **Autologous Donations**:
    - Patients shall fully understand the risks and benefits of their donation.
    - Ethical concerns regarding informed consent and risks of using one's own cells when alternatives may exist.

APPENDIX 5: HEMATOPOIETIC STEM CELLS (HSC)

- **Bone Marrow Aspiration:** The procedure shall be conducted under sterile conditions by qualified healthcare professionals, following DHA standard for donor safety and pain management.
- **Peripheral Blood Stem Cells:** Leukapheresis, using G-CSF mobilization, shall follow DHA-approved protocols, ensuring donor safety and optimized stem cell yield.
- **Umbilical Cord Blood:** Collection shall occur under aseptic conditions immediately after delivery, following DHA's stringent timing and procedural standard to ensure cell yield and safety.

Mesenchymal Stem Cells (MSC):

- **Umbilical Cord/Placenta:** MSC collection from Wharton's jelly or placental tissue shall follow DHA's sterile procedures to maximize yield and viability.
- **Adipose Tissue:** Liposuction techniques for MSC collection shall meet DHA's safety standards to ensure minimal risk to the donor and optimal cell viability.
- **Dental Pulp:** Protocols shall be followed to preserve cell integrity during collection from extracted teeth.
- **Amniotic Fluid and Membrane:** Collection during cesarean or amniocentesis shall adhere to DHA's aseptic protocols.
- **Exosome Harvesting:** Exosome harvesting from MSC culture shall be validated under DHA-approved conditions to maintain integrity.

Autologous Stem Cell Sources

- **Autologous** stem cells are derived from the same patient who will receive the treatment.
- As these stem cells are from the patient's own body, they avoid complications like immune rejection or graft-versus-host disease (GVHD), making them an attractive option for various therapies.

Advantages of autologous stem cells

- **No Immune Rejection:** Since the stem cells are from the patient's own body, there is no risk of immune rejection.
- **Lower Risk of GVHD:** Autologous stem cells eliminate the risk of GVHD.
- **Ethical Considerations:** There are no ethical concerns related to donor consent or the use of embryonic stem cells, as the patient's own cells are used.