# NATIONAL REGULATORY FRAMEWORK
# FOR HUMAN CELL AND GENE THERAPY
## (ISLAMIC REPUBLIC OF PAKISTAN)

## Chapter 1. GUIDELINES FOR HUMAN CELL (STEM CELL) THERAPY

### PART I – PREAMBLE, OBJECTIVES, LEGAL BASIS, AND SCOPE

**Article 1 – Preamble**

Recognizing the increasing clinical, therapeutic, and scientific use of human tissues, stem cells, and advanced cellular therapies, and acknowledging the significant risks to human health, safety, dignity, and public trust arising from unregulated, inadequately controlled, or commercially motivated practices, this Regulation establishes a unified national regulatory framework governing all activities involving human tissues and cells.

This Regulation aims to ensure that all such activities are conducted in accordance with the highest standards of quality, safety, ethics, traceability, scientific validity, and accountability, while aligning national practice with internationally recognized regulatory frameworks and preserving Pakistan's legal, ethical, cultural, and religious values.

**Article 2 – Objectives**

The objectives of this Regulation are to:

2.1 Ensure the HOTA-led regulation of donation, procurement, and clinical application, while maintaining DRAP-led oversight for industrial processing and manufacturing standards of derived products.

2.2 Establish mandatory quality and safety standards to ensure the highest level of protection of human health and patient safety;

2.3 Define authorization, licensing, infrastructure, personnel, equipment, documentation, and operational standards for tissue and cell centers, procurement establishments, testing laboratories, storage facilities, and service providers

2.4 Ensure ethical donation, voluntary participation, informed consent, and full protection of donor and recipient rights;

2.5 Establish traceability, vigilance, recall, reporting, and corrective action systems covering the entire lifecycle of tissues and cells

2.6 Provide a clear and enforceable regulatory separation between:

2.6.1 Human stem cells (Adipose derived Mesenchymal stem cells ADSCs, Bone Marrow Mesenchymal Stem Cells BM-MSCs, Hematopoietic Stem cells HSCs, Umbilical Cord Derived Stem Cells UCSCs etc) and related products except for embryonic stem cells for approved clinical indications by reference regulatory authorities will be regulated by HOTA.

2.6.2 Advanced therapy medicinal products (ATMPs) which includes any cell or gene therapy product or tissue engineered product that has been substantially manipulated and/or performs a different function in the recipient than in the donor. ATMPs are usually produced from genetically modified and/or substantially manipulated somatic cells or tissues. ATMPs also include nucleic

acids, viral and non-viral vectors, recombinant bacterial cells and recombinant oncolytic viruses. ATMPs shall be regulated by the Drug Regulatory Authority of Pakistan.
2.7 Prevent misuse, unethical commercialization, misleading therapeutic claims, unsafe practices, and the clinical use of unproven or experimental cellular therapies outside approved regulatory pathways.

**Article 3 – Scope of Application**
3.1 Included Activities
This Regulation applies to all public and private institutions, establishments, real and legal persons involved in:
3.1.1 Donation and procurement of human tissues and cells;
3.1.2 Testing, processing, expansion, preservation, storage, banking, labeling, documentation, and distribution
3.1.3 Clinical application of stem cell based therapies
3.1.4 Activities of tissue and cell centers, procurement establishments, testing laboratories, storage facilities, and distribution entities
3.1.5 Advanced therapy medicinal products (ATMPs).
3.2 Exclusions
This Regulation does not apply to:
3.2.1 Autologous tissues or cells:
obtained without more than minimal manipulation
used without prior storage; and
re-administered within the same surgical procedure
3.2.2 Whole blood or blood components or blood derivative products
3.2.3 Solid organs or parts of organs intended to perform the same essential function as the whole organ
Cells, tissues, or organs obtained from animal sources. Secreted or extracted human products, such as milk, collagen, and cell factors; except that semen is considered an HCTs. Ancillary products used in the manufacture of HCT's. HCT's solely for nonclinical scientific or educational purposes
In vitro diagnostic products;
**Article 4 – Legal Basis**
This Regulation is enacted pursuant to:
4.1 National and provincial health, transplantation, and drug regulatory laws of Pakistan
4.2 The statutory mandate of the Human Organ Transplant Authority (HOTA);
4.3 The statutory mandate of the Drug Regulatory Authority of Pakistan (DRAP);
4.4 European Union Regulatory Framework, including:

- Directive 2004/23/EC on standards of quality and safety for the donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells;
- Commission Directive 2006/17/EC on technical requirements for donation, procurement, and testing;
- Commission Directive 2006/86/EC on traceability, notification of serious adverse reactions and events, and coding requirements;

4.5 World Health Organization (WHO) instruments, including the WHO Guidelines on Human Cell and Tissue Transplantation and related technical guidance;
4.6 United States Food and Drug Administration (US FDA) Regulatory Framework, including:

• Title 21 of the Code of Federal Regulations (21 CFR), particularly Parts 1271 (Human Cells, Tissues, and Cellular and Tissue-Based Products), 210, 211 (Good Manufacturing Practice), 312 (Investigational New Drug Application), and 601 (Biologics License Application)

• FDA guidance documents applicable to cellular and gene therapy products;

4.7 Japan's Regenerative Medicine Regulatory Framework, including:

• The Act on the Safety of Regenerative Medicine (ASRM)

• The Pharmaceuticals and Medical Devices Act (PMD Act), as administered by the Pharmaceuticals and Medical Devices Agency (PMDA)

4.8 Republic of Korea Regulatory Framework, including:

• The Act on the Safety of and Support for Advanced Regenerative Medicine and Advanced Biopharmaceuticals

• Regulatory guidance issued by the Ministry of Food and Drug Safety (MFDS);

## PART II – DEFINITIONS

**For the purposes of this Regulation:**

Cells – Individual human cells or a collection of human cells not bound by connective tissue.
Stem Cells - Stem cells are cells characterized by their ability to self-renew through mitotic cell division and to differentiate into a diverse range of specialized cell types under appropriate biological conditions.
Tissue – Any constituent part of the human body formed by cells.
Donor – Any human source, living or deceased, of tissues or cells.
Donation – The act of donating human tissues or cells intended for human applications.
Organ – A differentiated and vital part of the human body with autonomous physiological function.
Autologous – Tissue or cells procured from and administered to the same individual.
Allogeneic – Tissue or cells procured from one individual and administered to another.
Minimal manipulation - Minimal manipulation means: 1) For structural tissue, processing that does not alter the original relevant characteristics of the tissue relating to the tissue's utility for reconstruction, repair, or replacement; 2) For cells or nonstructural tissues, processing that does not alter the relevant biological characteristics of cells or tissues. Section 1271.10(a)(1) (21 CFR 1271.10(a)(1)) under section 361 of the PHS Act and the regulations in Part 1271
Procurement – The process by which tissues or cells are made available.
Processing – All operations involved in preparation, manipulation, preservation, and packaging.
Preservation – Use of chemical agents or environmental control to prevent biological deterioration.
Quarantine – Physical or effective isolation pending acceptance or rejection.
Storage – Maintenance under controlled conditions until distribution.
Distribution – Transportation and delivery for human application.
Human Application – Use on or in a human recipient, including extracorporeal use.
Serious Adverse Event – Any occurrence that may lead to disease transmission, death, disability, or hospitalization.
Serious Adverse Reaction – An unintended response in donor or recipient that is fatal, disabling, or life-threatening.

Traceability – Ability to track tissues and cells from donor to recipient and vice versa.
Quality Management System (QMS) – Organizational structure, procedures, responsibilities, and resources ensuring quality.
Tissue and Cell Center – Establishment authorized to procure, test, process, store, and distribute tissues and cells.
Cadaveric Donor – A non-living human source of tissues or cells.
Standard Operating Procedure (SOP) – Written instructions describing all critical processes.
Reproductive Cells – Cells and tissues used in in-vitro fertilization.
Validation – Demonstration that systems, methods, or equipment perform as intended.
Approved Product - Cell–based products that have been reviewed, validated, and authorized by the relevant regulatory authority for manufacturing, storage, and clinical use in accordance with applicable laws, GMP standards, and ethical guidelines.
Approved Indications - Specific diseases, conditions, or clinical applications for which the use of approved cell products has been formally evaluated and permitted by the reference regulatory authorities based on evidence of safety and efficacy.

## PART III – TISSUE AND CELL (STEM CELL) FACILITIES

### Article 5 – Establishment, Authorization, and Functional components of Cell and Tissue Facilities

5.1 Establishment of TISSUE AND CELL (STEM CELL) Facilities
Accredited and approved TISSUE AND CELL (STEM CELL) facilities may be established by:
a) Universities and academic medical institutions
b) Public sector hospitals, research institutes, and health organizations
c) Private legal entities duly registered under the laws of Pakistan
d) Real persons, subject to full compliance with all legal, technical, ethical, and regulatory requirements of this Regulation.

5.2 General Authorization Requirement
No TISSUE AND CELL (STEM CELL) facility shall commence or continue operations unless it has obtained prior written authorization and licensing from the competent authority in accordance with this Regulation. Authorization shall define the approved scope of activities, and the facility shall operate strictly within that scope.

### Article 6 Functional components of Cell and Tissue Facilities:

All licensed TISSUE AND CELL (STEM CELL) facilities shall be capable of establishing, maintaining, or formally contracting the following functional components in compliance with this Regulation:

1. Procurement of human tissues and cells
2. Screening or testing of the cell or tissue
3. Processing and expansion
4. Testing and quality control
5. Storage and tissue/cell banking;
6. Distribution and supply.

Such functions may be performed within a single establishment or through authorized third parties, provided that traceability, quality responsibility, and regulatory accountability are fully maintained

**6.1 Procurement of Human Tissues and Cells**

6.1.1 Donation Principles

Donation of human tissues and cells shall be:

- Voluntary and Non-Commercial Donation
- Voluntary, altruistic, and free of charge.

6.1.1.1 No form of payment, financial reward, or material benefit shall be offered or provided to donors.

6.1.1.2 Only obligatory and documented expenses related to the donation process may be covered by the donor.

6.1.1.3 Promotion and Awareness Activities:

- Public awareness and educational activities to promote tissue and cell donation shall be organized, authorized, or supervised by DRAP or another competent authority designated by law.

6.1.1.4 All promotional activities shall: (Be regulated by HOTA) HOTA COMMENTS NEEDED

- Be factual, ethical, and non-misleading
- Respect human dignity and donor autonomy
- Avoid therapeutic exaggeration or unrealistic expectations
- Any form of promotion, advertisement, or solicitation that promises material gain, preferential treatment, or other benefits in exchange for donation is strictly prohibited.
- The commercialization, brokerage, or trade of human tissues and cells is prohibited under this Regulation
- All donation-related activities shall be subject to regulatory oversight, audit, and enforcement
- Violations of this Article shall constitute grounds for administrative action, suspension of authorization, or other penalties under applicable law.

6.1.1.5 All donation-related activities shall be subject to regulatory oversight through a structured mechanism that includes authorization of procurement facilities, adherence to approved standard operating procedures, routine and risk-based audits, review of donor records and traceability documentation, and enforcement actions by the competent authority in accordance with applicable legal and regulatory requirements.

6.1.2 Authorization and Personnel Qualification

6.1.2.1 Procurement personnel shall have:

a) Successfully completed formal training

b) Demonstrated competence in clinical, technical, and ethical aspects of procurement;

c) Undergone periodic refresher training and competency reassessment.

**6.1.3 Donor Selection and Eligibility**

6.1.3.1 Donors shall be evaluated based on:

a) Approved eligibility criteria

b) Medical and behavioral risk assessment;

c) Mandatory infectious disease screening;

d) Ethical review and approval, where applicable.
6.1.3.2 Procurement shall not proceed unless donor eligibility is confirmed and documented.

**6.1.4 Informed Consent**
6.1.4.1 Written informed consent shall be obtained prior to procurement from the donor or legally authorized representative.
6.1.4.2 Consent shall include, at minimum:
a) Purpose and nature of donation
b) Type of tissues or cells procured
c) Potential risks and discomforts
d) Intended clinical or research use
e) Storage duration and future use options
f) Right to withdraw consent, where applicable
g) Confidentiality and data protection measures.
**6.1.5 Procurement Procedures**
6.1.5.1 Procurement personell shall:
a) Use aseptic techniques and validated medical devices
b) Minimize contamination and donor risk;
c) Respect donor safety, dignity, and privacy.
6.1.5.2 Procedures shall be conducted in appropriate clinical environments equipped to manage complications.
**6.1.6 Documentation and Traceability**
6.1.6.1 Each procurement event shall be fully documented, including:
a) Donor identification and eligibility
b) Date, time, and location
c) Personnel involved
d) Type and quantity procured
e) Unique donor and product identification codes.
6.1.6.2 Traceability from donor to recipient shall be appropriately maintained.
**6.1.7 Packaging, Labeling, and Transportation**
6.1.7.1 Post-procurement materials shall be packaged in validated, sterile, leak-proof containers and labeled using approved identification systems.
6.1.7.2 Transportation shall be conducted under validated cold-chain conditions with continuous monitoring and documented chain-of-custody.
**6.1.8 Prohibited Practices**
The following are strictly prohibited:
a) Procurement without informed consent;
b) Procurement by unauthorized or untrained personnel;
c) Commercialization or inducement of donation;
d) Procurement outside authorized facilities or protocols.
**6.1.9 Oversight and Compliance**
Procurement activities shall be subject to inspection, audit, and oversight. Any serious adverse events, deviations, or non-compliance shall be reported without delay.

**Article 6.2 – Processing and Expansion**

TISSUE AND CELL (STEM CELL) facilities shall perform processing and expansion activities in accordance with validated SOPs and a documented Quality Management System. Activities may include isolation, washing, separation, preparation, and approved ex vivo expansion.

6.2.1 Processing shall:

- Be conducted only in DRAP-certified GMP facilities and limited to the approved therapies by HOTA.
- Be conducted under controlled environmental conditions appropriate to the manipulation level.
- Follow validated SOPs with defined critical control points.
- Minimize time between procurement and processing to preserve cell viability.

6.2.2 Environmental Control:

Environmental monitoring for particulates, viable counts, pressure differentials, and cleaning efficacy.

6.2.3 Processing Controls

- Defined maximum processing time.
- Validated centrifugation speeds and durations
- Use of qualified reagents and consumables
- Segregation of quarantined, released, and rejected material
- Any deviation shall trigger investigation and CAPA prior to release.

**6.2.4 Cell Expansion (Where Approved)**

6.2.4.1 Authorization

Cell expansion shall be permitted only for approved products and shall be conducted exclusively in DRAP-certified GMP facilities.

6.2.4.2 Culture Conditions

SOPs shall define:

- Cell source and passage limits
- Culture media composition and supplementation

6.2.4.3 Incubation conditions shall be as follows:

- Temperature: 36–37°C
- CO2: 5 ± 1%
- Humidity: ≥ 90%

6.2.4.4 In-Process Controls shall ensure:

- Daily morphological assessment
- Viability monitoring
- Microbial surveillance during culture
- Defined criteria for culture continuation or termination

6.2.4.5 Expansion limits will be as per given criteria:

- Maximum population doublings or passage number shall be predefined
- Expanded cells exceeding limits shall not be released for clinical use

**6.3 Testing and Quality Control**

6.3.1 TISSUE AND CELL (STEM CELL) facilities shall ensure access to internally integrated quality control laboratories for:

- Donor screening and infectious disease testing, Identity, viability, sterility, endotoxin, and potency testing, as applicable
- Method validation and quality record maintenance
- Reporting of deviations, out-of-specification results, and adverse findings.

**6.4 Storage and Tissue/Cell Banking:**

6.4.1 Facilities shall store tissues and cells under validated, continuously monitored conditions and ensure:

- Inventory control and segregation by product status
- Long-term record retention in accordance with traceability requirements.

6.4.2 Short-Term Storage:

- Fresh tissues/cells should be stored at: +2°C to +8°C
- Maximum holding time should be defined per product

6.4.3 Cryopreservation

- Controlled-rate freezing mandatory
- Cooling rate: –1°C to –2°C per minute
- Use of validated cryoprotectants

6.4.4 Long-Term Storage:

- Vapor-phase liquid nitrogen: ≤ –150°C
- Liquid nitrogen (where justified): ≤ –196°C
- Continuous temperature monitoring
- Alarm systems and emergency response plans
- Redundant storage or disaster recovery strategy

**6.5 Distribution and Supply**

6.5.1 All the TISSUE AND CELL (STEM CELL) facilities shall manage the release and distribution of cellular (stem cells) and gene therapy products by ensuring:

- Validated cold-chain logistics
- Chain-of-custody documentation
- Coordination with authorized clinical facilities
- Confirmation of receipt and use.

All steps in the recovery, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and the screening or testing of the cell or tissue donor shall be conducted in HOTA licensed and DRAP GMP facilities.

**6.6 ISO Class 5 Clean Rooms**

Critical aseptic activities such as processing, cultivation, manipulation, harvesting, aseptic filling shall be performed in controlled environments consistent with ISO 14644-1 Class 5 (Grade A) cleanrooms (or equivalent) to minimize particulate and microbial contamination.”.

**6.7 Power Backup and Continuity of Critical Operations**

- Appropriate, readily available, and integrated backup power supply system shall be maintained to ensure uninterrupted operation.
- The backup system shall be capable of automatic switchover

**6.8 Obligations of TISSUE AND CELL (STEM CELL) Facilities**

6.6.1 TISSUE AND CELL (STEM CELL) facilities shall:

- Establish a defined organizational and operational structure;
- Maintain a documented Quality Management System
- Identify and mitigate biological, environmental, and personnel risks;
- Ensure third-party agreements do not dilute regulatory responsibility;
- Maintain document control, traceability, and release systems
- Ensure continuity of traceability if operations cease
- Conduct donor testing only in qualified laboratories.

**Article-7 Personnel and Responsible Person**

7.1 Each center shall appoint responsible persons with relevant medical or biological sciences qualifications and practical experience.

7.2 Duties of the personnel and responsible persons shall include:

- Ensuring compliance with approved regulations
- Establishing and maintaining QMS
- Reporting serious adverse events
- Coordinating with competent authorities
- Ensuring staff training, competence, and ethical awareness.

**7.3 Staff Qualifications and Responsibilities**

7.3.1 General Staffing Requirements

TISSUE AND CELL (STEM CELL) facilities shall appoint a sufficient number of personnel with appropriate qualifications, training, and experience commensurate with the activities they perform. Licensing Authority (HOTA) shall determine qualification and also approve the responsible personnel for activities performed under the license.

7.3.2 Responsible Person (Head of the Facility)

Each TISSUE AND CELL (STEM CELL) facility shall appoint a Responsible Person (RP) who shall have relevant practical experience in the field corresponding to the authorized activities of the facility.

A degree in medicine, biological sciences, or a related discipline, including graduates of undergraduate, postgraduate, or doctoral programs relevant to the facility's scope of work
Full-time employment at the facility.

The Responsible Person shall have overall authority and accountability for regulatory compliance.

7.3.3 Duties of the Responsible Person

The Responsible Person shall be responsible for:

a) Ensuring that human tissues and cells are procured, tested, processed, stored, and distributed in accordance with this Regulation and applicable legislation;

b) Providing required information and reports to the competent authorities;

c) Establishing, implementing, and maintaining the Quality Management System (QMS)
d) Reporting serious adverse events and reactions without delay
e) Ensuring staff competency, training, and compliance with approved procedures.
7.3.4 Staffing Framework for Clinical Stem Cell Facility

**7.3.4.1. Laboratory Director / Head of Manufacturing**
Minimum Qualification:
PhD in Regenerative Medicine/Molecular Biology with research in Stem Cells/regenerative medicine or M.phil in Molecular Biology with research in stem cells/Regenerative Medicine with minimum 4 years of clinical experience in stem cells/regenerative medicine
Role & Responsibilities:
Responsible for overall manufacturing strategy, validation of processes, deviation management, and technical supervision of laboratory operations. Ensures personnel qualification, aseptic compliance, and process integrity. Must function independently from routine processing staff.

**7.3.4.2. Quality Assurance (QA) Manager**
Minimum Qualification:
Phd/M.phil in Regenerative Medicine/Molecular Biology with experience (For M.phil minimum 2 years clinical stem cell experience) in Stem Cells/Regenerative Medicine/Biopharmaceutical and well aware with quality assurrance management
Role & Responsibilities:
Owns the Quality Management System (QMS), including SOP control, audits, CAPA, change control, training documentation, and batch record review. Authorizes product release in coordination with the Medical and Laboratory Directors. Must be independent of manufacturing operations.

**7.3.4.3. Quality Control (QC) Analyst**
Minimum Qualification: BS.Hons in Microbiology/Medical Laboratory Sciences/Medical Laboratory Technology/Biotechnology or equivalent
Role & Responsibilities:
Performs or oversees sterility testing, endotoxin, mycoplasma, viability, identity (flow cytometry), potency-related assays, and environmental monitoring. Generates QC data to support product release decisions.

**7.3.4.4. Cell Processing Technologists/Scientists**
Minimum Qualification:
M.phil in Regenerative Medicine/Molecular Biology/Cell Biology or equivalent with minimum two years of clinical stem cell experience.
Role & Responsibilities:
Conduct sample receipt and chain-of-identity verification, stem cell isolation from cord blood, adipose tissue, or bone marrow, cell expansion, harvesting, formulation, cryopreservation, and aseptic processing under GMP conditions.

**7.3.4.5 Collection / Procurement Team**
Minimum Qualification:
Clinical Coordinator: BSc Nursing or Allied Health Sciences.

Physicians: MD with procedure-specific training.
Role & Responsibilities:
Coordinates and performs tissue procurement. Cord blood collections are conducted by obstetricians or trained midwives; bone marrow collections by hematologists with anesthetic support; adipose tissue collections by trained physicians or surgeons with anesthetist support. The clinical coordinator manages donor screening, informed consent, and transport documentation.

**7.3.4.6. Apheresis / Collection Technologist (If Applicable) (1)**
Minimum Qualification:
Certified apheresis technologist or trained registered nurse.
Role & Responsibilities:
Operates apheresis equipment, monitors donors, ensures proper labeling and traceability, and maintains compliance with ISBT-128 standards where applicable

**7.3.4.7. Regulatory Affairs / Documentation / Data Manager**
**Minimum Qualification**:
BA/BS Hons or equivalent with experience in regulatory affairs, documentation control, and quality systems.
**Role & Responsibilities:**
Manages regulatory submissions, batch and release documentation, electronic records (LIMS), audit preparation, and long-term data retention in compliance with regulatory requirements.
**7.3.4.8. Job Descriptions and Organizational Structure**

- The facility shall establish and maintain clear, current, and documented job descriptions for all personnel.
- Staff responsibilities shall be formally documented, and personnel shall acknowledge understanding of their assigned duties.

**7.5 Training and Competency**
All personnel shall receive:

- Initial baseline training prior to performing assigned duties;
- Periodic refresher training in response to updates in SOPs, scientific knowledge, or regulatory requirements.

7.5.1 The facility shall ensure and document that personnel:
a) Are competent to perform their assigned duties
b) Understand relevant scientific and technical principles
c) Are familiar with the organizational structure, QMS, and health and safety requirements;
d) Are informed of the ethical, legal, and professional responsibilities associated with their roles.

**Article 8 – Equipment and Materials**
All equipment shall be:
8.1 Qualified, validated, calibrated, and maintained;
8.2 Documented and monitored;
8.3 Supported by SOPs addressing7 failures and corrective actions;
8.4 Used with validated critical reagents and materials.

**Article 9 – Documentation and Records**

Centers shall maintain:

9.1 Approved SOPs and controlled documents

9.2 Accurate, indelible records

9.3 Records retained

9.4 Confidentiality and controlled access systems.

**Article 10 – Quality Management and Audits**

10.1 Quality management and audit team will:

Maintain an active QMS

- Conduct internal audits
- Implement corrective and preventive actions (CAPA)
- Prepare for regulatory inspections.

10.2 Inspection and Control Measures

10.2.1 Competent Inspection Authorities

The Drug Regulatory Authority of Pakistan (DRAP) and the Human Organ Transplant Authority (HOTA) shall exercise inspection and oversight within their respective regulatory mandates under this Regulation.

10.2.2 DRAP shall inspect facilities and laboratories involved in donar noscreening/testing, processing, expansion, storage, quality control, and activities requiring GMP compliance.

10.2.3 HOTA shall inspect activities related to donor eligibility, procurement, ethical compliance, traceability, clinical use, and post-treatment monitoring of cellular (Stem cell) therapies

10.2.4 Routine Inspections

The frequency of inspection shall be at DRAP & HOTA discretion, which may include routine inspections and for cause and unannounced inspections.

10.2.5 Routine inspections shall include:

- Verification of compliance with the standards and requirements of this Regulation
- Review of facilities, processes, and operational controls
- Examination of all relevant documents, records, and traceability systems.

10.2.6 Personnel Conducting Inspections

- The qualification, training, authorization, and assignment of inspectors shall be determined by the respective competent authority.
- Inspectors shall possess appropriate technical, scientific, and regulatory expertise relevant to the scope of inspection.

10.2.7 For-Cause and Unannounced Inspections

In addition to routine inspections, for-cause or unannounced inspections may be conducted where:

- A serious adverse event or reaction is reported;
- Significant non-compliance is suspected;
- Required by public health considerations
- Requested through international cooperation, mutual recognition, or information exchange with foreign regulatory authorities.

10.2.8 Cooperation and Enforcement (Essential Clarification)

Cell and Tissue Facilities shall:

- Grant inspectors full access to premises, records, and personnel
- Cooperate fully during inspections and audits;
- Implement corrective and preventive actions within specified timelines.

10.2.9 Failure to comply with inspection findings may result in:

- Regulatory action, including suspension or revocation of authorization, without prejudice to other legal penalties.

## PART 4 LICENSING AND APPROVAL OF TISSUE AND CELL FACILITIES

**Article 11 Licensing Authorities and roles:**

11.1The Human Organ Transplant Authority (HOTA) shall be the primary authority for the licensing, authorization, and oversight of-TISSUE AND CELL (STEM CELL) facilities engaged in cellular (Stem Cells) and gene therapies.

HOTA approval and GMP/GTP certification from DRAP shall be mandatory for procurement, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and the screening or testing of the cell or tissue donor.

11.2 Relevant regulatory authorities will ensure:

- Approval of treatment indications and protocols
- Ethical compliance, donor eligibility, and traceability
- Intended approved clinical use of stem cells and related products are permitted under HOTA oversight.
- Allogeneic use shall require enhanced donor screening, traceability, and post-treatment monitoring.
- Tissue and cells (stem cells) shall be processed only in DRAP-certified GMP facilities and require prior written approval from HOTA before clinical use.

11.3 *Note: Registration of all genetically engineered, gene-edited, or vector-modified cellular products and Advanced Therapy Medicinal Products (ATMPs) fall under DRAP jurisdiction whereas the clinical and therapy related approvals of said products fall under HOTA jurisdiction

### Article 12 – Permitted TISSUE AND CELL (STEM CELL) Sources and Use

**12.1 Permitted Sources**

Following human tissue and cell (stem cell) sources upon subject to approval are permitted:
Adipose tissue
Bone marrow
Peripheral blood
Umbilical cord blood
Umbilical cord tissue (Wharton’s Jelly) and other approved cell sources.

**12.2 Prohibited Sources**

Use of embryonic stem cells for research or therapy in humans is strictly prohibited.

**CHAPTER 2- GENE THERAPY (ADVANCE THERAPY MEDICINAL PRODUCTS)**

**(STRICT DRAP REGULATORY FRAMEWORK)**

Advanced therapy medicinal product (ATMP) - Any cell or gene therapy product or tissue engineered product that has been substantially manipulated and/or performs a different function in the recipient than in the donor. ATMPs are usually produced from genetically modified and/or substantially manipulated somatic cells or tissues. ATMPs also include nucleic acids, viral and non-viral vectors, recombinant bacterial cells and recombinant oncolytic viruses. Xenogeneic cells and tissues are included in the definition of ATMPs but are not within the scope of this document due to the complexity of their application.

ATMPs product registration shall be exclusively licensed by DRAP. Products manufactured at such facilities shall be registered as biological products based on comprehensive data demonstrating quality, safety, and efficacy, while taking into account approvals and regulatory guidelines established by reference regulatory authorities.

All registered Advanced Therapy Medicinal Products (ATMPs) shall be subject to the clinical and ethical oversight of HOTA. The clinical administration, application, or practice of such products shall be permitted exclusively within healthcare facilities duly licensed by HOTA in accordance with the applicable laws and regulations

DRAP will provide and integrate the complete regulatory frame work for ATMPs to the facilities as the integral part of this document.