EU directive to raise standards of transplant tissue to highest-ever levels

EU Matters

Editor's Note: In last month’s issue, we looked at the implications for ophthalmologists resulting from the European Union’s newly adopted Second Technical Directive on Human Tissue, which will introduce a new coding and traceability system for corneal tissue and other ocular tissue used in transplants. In this month’s issue, we continue our examination of the second technical directive and its effect on how eye banks process, store and distribute tissue.

The European Union’s newly adopted Second Technical Human Tissue Directive, which will introduce a new coding and traceability system for transplanted corneas over the next year, will also introduce state-of-the-art standards for the tissue banks that process, store, and distribute such tissue. Those new standards will affect every tissue bank in every EU country – from the qualifications of the director of the bank and personnel who run the bank to the premises in which the tissue bank operates and the equipment it uses.

Operational requirements

The EU’s Second Technical Human Tissue Directive requires that each tissue bank follow a number of standards in running its business, including the following:

1. Hiring only a qualified person at its head.
2. Implementing an organisational structure and operational procedures appropriate to the activities for which accreditation, designation, authorisation, or licensing is sought.
3. Nominating a physician to advise on and oversee the establishment’s medical activities such as donor selection, review of clinical outcomes of applied tissues and cells or interaction as appropriate with clinical users.
4. Applying a documented quality management system to the activities for which accreditation, designation, authorisation, or licensing is sought, in accordance with the standards laid down in the directive.
5. Ensuring that the risks inherent in the use and handling of biological material are identified and minimised, consistent with maintaining adequate quality and safety for the intended purpose of the tissues and cells.
6. Making agreements with other tissue banks only under terms consistent with EU law and the requirements of the directive.
7. Maintaining a documented system, supervised by the head of the tissue bank, for ratifying that human tissues and cells meet appropriate specifications for safety and quality for release and for their distribution.
8. Have a documented system in place that ensures the identification of every unit of tissue or cells at all stages of the activities for which accreditation, designation, authorisation, or licensing is sought.

Personnel and training provisions

The directive also requires specific guidelines for the staff that the tissue bank hires and how they perform their jobs, including:

1. Personnel in tissue banks must be available in sufficient numbers and be qualified for the tasks they perform;
2. Competency of the personnel must be evaluated at appropriate intervals specified in the quality system;
3. Personnel should have clear, documented, and up-to-date job descriptions;
4. Personnel must be provided with basic training, updated training as required when procedures change or scientific knowledge develops and adequate opportunities for relevant professional development;
5. A training programme that must ensure and document that each individual:
(a) has demonstrated competence in the performance of their designated tasks;
(b) has an adequate knowledge and understanding of the scientific/technical processes and principles relevant to their designated tasks;
6. A training programme that must ensure and document that each individual:
(a) has demonstrated competence in the performance of their designated tasks;
(b) has an adequate knowledge and understanding of the scientific/technical processes and principles relevant to their designated tasks;
(c) understands the organisational framework, quality system and health and safety rules of the establishment in which they work;
(d) is adequately informed of the broader ethical, legal, and regulatory context of their work.

Equipment and material protocols

The directive lays down specific requirements for the equipment and materials used by tissue banks. For example:

1. All equipment and material must be designed and maintained to suit its intended purpose and must minimise any hazard to recipients and/or staff.
2. All critical equipment and technical devices must be identified and validated, regularly inspected and preventively maintained in accordance with the manufacturers’ instructions. Where equipment or materials affect critical processing or storage parameters (e.g., temperature, pressure, particle counts, microbial contamination levels), they must be identified and must be the subject of appropriate monitoring, alerts, alarms and corrective action, as required, to detect malfunctions and defects and to ensure that the critical parameters are maintained within acceptable limits at all times. All equipment with a critical

EU directive raises standards for processing, storage, and distribution of cornea

As part of its focus on improving the quality and safety of corneas and transplant tissue, the second technical human tissue directive requires tissue banks to follow strict protocols in processing, storing, and distributing such tissue.

Those requirements include:

Processing:

(a) Critical processing procedures must be validated and must not render the tissues or cells clinically ineffective or harmful to the recipient. This validation may be based on studies performed by the establishment itself, or on data from published studies or, for well-established processing procedures, by retrospective evaluation of the clinical results for tissues supplied by the establishment.
(b) All processes must be conducted in accordance with the approved standard operating procedures.
(c) Where a microbial inactivation procedure is applied to the tissue or cells, it must be specified, documented, and validated.
(d) Procedures for discarding tissue and cells must prevent the contamination of other donations and products, the processing environment or personnel. These procedures must comply with national regulations.

Storage:

(a) Maximum storage time must be specified for each type of storage condition. The selected period must reflect among others possible deterioration of the required tissue and cell properties.
(b) There must be a system of inventory hold for tissues and cells to ensure that they cannot be released until all requirements laid down in this directive have been satisfied. There must be a standard operating procedure that details the circumstances, responsibilities, and procedures for the release of tissues and cells for distribution.
(c) A system for identification of tissues and cells throughout any phase of processing in the tissue establishment must clearly distinguish release from quarantined and discarded products.
(d) Records must demonstrate that before tissues and cells are released all appropriate specifications are met, in particular all current declaration forms, relevant medical records, processing records and test results have been verified.

Distribution:

(a) Critical transport conditions, such as temperature and time limit must be defined to maintain the required tissue and cell properties. The container/package must be secure and ensure that the tissue and cells are maintained in the specified conditions.
(b) All containers and packages need to be validated as fit for the purpose for which they are used.
(c) Where distribution is carried out by a contracted third party, a documented agreement must be in place to ensure that the required conditions are maintained.
(d) There must be personnel authorised within the tissue establishment to assess the need for recall and to initiate and coordinate the necessary actions.
(e) An effective recall procedure must be in place, including a description of the responsibilities and actions to be taken. This must include notification to the competent authority in each country.
Learn more about how the EU’s human tissue directives may affect your practice

To find out more information about the effects of the human tissue directives on your practice, see:

Main Human Tissue Directive:

Technical Human Tissue Directive 1:

Technical Human Tissue Directive 2:

measuring function must be calibrated against a traceable standard if available.

3. New and repaired equipment must be tested when installed and must be validated before use. Test results must be documented.

4. Maintenance, servicing, cleaning, disinfection, and sanitation of all critical equipment must be performed regularly and recorded accordingly.

5. Procedures for the operation of each piece of critical equipment, detailing the action to be taken in the event of malfunctions or failure, must be available.

6. The procedures for the activities for which accreditation, designation, authorisation, or licensing is sought, must detail the specifications for all critical materials and reagents. In particular, specifications for solutions and packaging materials must be defined. Critical reagents and materials must meet documented requirements and specifications and when applicable the requirements of European law.

Facility and air quality rules

The directive even goes so far as to make specific rules about the type of facility the tissue banks must operate, with particular attention to the air quality of the bank. For instance:

1. A tissue establishment must have suitable facilities to carry out the activities for which accreditation, designation, authorisation, or licensing is sought, in accordance with the standards laid down in this directive.

2. When these activities include processing of tissues and cells while exposed to the environment, this must take place in an environment with specified air quality and cleanliness in order to minimise the risk of contamination, including cross-contamination between donations. The effectiveness of these measures must be validated and monitored.

3. Where tissues or cells are exposed to the environment during processing, without a subsequent microbial inactivation process, an air quality with particle counts and microbial colony counts in line with the current European Guide to Good Manufacturing Practice are required.

4. It must be demonstrated and documented that the chosen environment achieves the quality and safety required, at least taking into account the intended purpose, mode of application and immune status of the recipient. Appropriate garments and equipment for personal protection and hygiene must be provided in each relevant department of the tissue establishment along with written hygiene and gowning instructions.

5. When the activities for which licensing is sought involve storage of tissues and cells, the storage conditions necessary to maintain the required tissue and cell properties, including relevant parameters such as temperature, humidity or air quality must be defined.

6. Critical parameters such as temperature, humidity, air quality must be controlled, monitored, and recorded to demonstrate compliance with the specified storage conditions.

7. Storage facilities must be provided that clearly separate and distinguish tissues and cells prior to their release or quarantine from those that are released and from those that are rejected, in order to prevent mix-up and cross-contamination between them. Physically separate areas or storage devices or secured segregation within the device must be allocated in both quarantine and released storage locations for holding certain tissue and cells collected in compliance with specific criteria.

8. The tissue establishment must have written policies and procedures for controlled access, cleaning and maintenance, waste disposal and for the re-provision of services in an emergency situation.

Mandatory documentation system

The second technical directive also specifies that tissue banks use an effective documentation system. For example:

1. There must be a system in place that results in clearly defined and effective documentation, correct records and registers and authorised Standard Operating Procedures, for the activities for which licensing is sought. Documents must be regularly reviewed and must conform to the standards laid down in this directive. The system must ensure that work performed is standardised, and that all steps are traceable.

2. For every critical activity, the materials, equipment, and personnel involved must be identified and documented.

3. In the tissue establishments all changes to documents must be reviewed, dated, approved, documented, and implemented promptly by authorised personnel.

4. A document control procedure must be established to provide for the history of document reviews and changes and to ensure that only current versions of documents are in use.

5. Records must be shown to be reliable and a true representation of the results.

6. Records must be legible and indeleble and may be handwritten or transferred to another validated system, such as a computer or microfilm.

7. All records, including raw data, which are critical to the safety and quality of the tissues and cells, shall be kept so as to ensure access to these data for at least 10 years after expiry date, clinical use, or disposal.

8. Access to registers and data must be restricted to persons authorised by the responsible person, and to the competent authority for the purpose of inspection and control measures.

Verifiable audit and quality review system

The second technical directive also mandates that every tissue bank audit its activities to ensure the quality and safety of its cornea and other tissue. To verify its quality and safety record, the directive specifies that:

1. An audit system must be in place for the activities for which accreditation, designation, authorisation, or licensing is sought. Trained and competent persons must conduct the audit in an independent way, at least every two years, in order to verify compliance with the approved protocols and the regulatory requirements. Findings and corrective actions must be documented;

2. Deviations from the required standards of quality and safety must lead to documented investigations which include a decision on possible corrective and preventive actions. The fate of non-conforming tissues and cells must be decided in accordance with written procedures supervised by the responsible person and recorded. All affected tissues and cells must be identified and accounted for;

3. Corrective actions must be documented, initiated, and completed in a timely and effective manner. Preventive and corrective actions should be assessed for effectiveness after implementation;

4. The tissue establishment should have processes in place for review of the performance of the quality management system to ensure continuous and systematic improvement.