HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to

Regulatory Requirements for the Procurement of Human Tissues and Cells intended for Human Application

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~~This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.~~

1 SCOPE

This guidance provides information in relation to the regulatory requirements for the procurement of human tissues and cells in Ireland. It is relevant to all stakeholders involved in any way with the procurement of human tissues and cells intended for subsequent human application.

2 LEGISLATION

Council Directive 2004/23/EC lays down standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. An associated Commission Directive, 2006/17/EC, sets out technical requirements for the activities of donation, procurement and testing of human tissues and cells and came into force on 1 November 2006. Both ~~of these Directives~~directives were transposed into Irish legislation via the European Communities (Quality and Safety of Human Tissues and Cells) Regulations 2006, (Statutory Instrument No.158 of 2006). ~~The Health Products Regulatory Authority (HPRA) is designated as the competent authority for the implementation of this legislation.~~

Another associated Commission Directive, 2006/86/EC, setting out the traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells, was published in October 2006 and has been transposed into Irish legislation via the European Communities (Human Tissues and Cells Traceability Requirements, Notification of Serious Adverse Reactions and Events and Certain Technical Requirements) Regulations 2007 (Statutory Instrument No. 598 of 2007).

Commission Directive (EU) 2015/565 of 8 April 2015 amending Directive 2006/86/EC as regards certain technical requirements for the coding of human tissues and cells, was transposed into Irish legislation via European Communities (Human Tissues And Cells Traceability Requirements, Notification Of Serious Adverse Reactions And Events And Certain Technical Requirements) (Amendment) Regulations 2019 (Statutory instrument No 32 of 2019).

Commission Directive (EU) 2015/566 of 8 April 2015 implementing Directive 2004/23/EC as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells, was transposed into Irish legislation via European Communities (Quality And Safety Of Human Tissues And Cells) (Amendment) Regulations 2019 (Statutory Instrument No. 33 of 2019.

The Health Products Regulatory Authority (HPRA) is designated as the competent authority for the implementation of this legislation.

3 DEFINITIONS

Tissue is defined as all constituent parts of the human body formed by cells.

Tissue establishment: a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. The establishment may also be responsible for procurement or testing of tissues and cells.

Procurement: a process by which tissue or cells are made available.

Procurement organisation: a healthcare establishment or a unit of a hospital or another body that undertakes the procurement of human tissues and cells and that may not be authorised as a tissue establishment.

Human application: the use of tissues or cells on or in a recipient and extracorporeal applications.

4 LEGISLATIVE REQUIREMENTS

The collection of tissues and cells intended for subsequent human application (e.g. umbilical cord stem cells, collection of skin cells for cosmetic uses) clearly falls within the definition of 'procurement' under EU and national legislation. Therefore, any entity involved in the procurement (and ~~also~~ in the testing, processing, preservation, storage and distribution) of human tissues or cells intended for human use is required to apply to the HPRA for an authorisation to perform such activities.

The HPRA's role is to ensure that tissue and cell procurement is carried out by persons with appropriate training and experience and that it takes place in conditions authorised for that purpose. The HPRA also ensures that appropriate control measures are in place for the procurement of human tissues and cells.

All authorised tissue establishments (and importing tissue establishments) are assigned an EU Establishment Code, available on the EU Tissue Establishment Compendium. The specific activities as authorised and other regulatory information are published on this compendium.

5 REGULATION OF PROCUREMENT

The HPRA regulates the procurement of human tissues and cells in two ways depending on where the tissue processing establishment is located:

1 The procurement site is supplying a tissue establishment in Ireland.
2 The procurement site is supplying a tissue establishment outside ~~the~~ Ireland.

In relation to 1 above, the act of procurement can be regulated through the inspection and authorisation of the Irish tissue establishment which processes the tissue or cells. In this scenario the procurement site does not need to be independently authorised but will be listed as a site of procurement on the tissue establishment's authorisation and will be inspected as part of the inspection of that tissue establishment.

In relation to 2 above, sites or organisations which procure tissues or cells for supply to tissue establishments outside Ireland are required to apply directly to the HPRA for authorisation. Thus, the harvesting in Ireland of tissues and cells intended for human application is subject to authorisation, even when not subsequently processed in Irish-based tissue establishments.

6 REQUIREMENTS FOR THE PROCUREMENT OF HUMAN TISSUES AND CELLS (DIRECTIVE 2006/17/EC, AS AMENDED)

The procurement of human tissues and cells is authorised only when the following requirements are met:

- Procurement of human tissues and cells is carried out by persons who have successfully completed a training programme specified by a clinical team specialising in the tissues and cells to be procured or a tissue establishment authorised for procurement.

- The tissue establishment or procurement organisation has written agreements with the staff or clinical teams responsible for donor selection, unless they are employed by the same organisation or establishment, specifying the procedures to be followed to assure compliance with the selection criteria for donors.

- The tissue establishment or procurement organisation has written agreements with the staff or clinical teams responsible for tissue/cell procurement, unless they are employed by the same organisation, specifying the type(s) of tissues and/or cells and/or samples for testing to be procured and the protocols to be followed.

- The tissue establishment shall designate a responsible person (RP) in line with the requirements of Article 8 of S.I. No. 158 of 2006, and this person shall be named on the authorisation.

- The tissue establishment shall establish and maintain a quality system based on the principles of good practice and in accordance with the requirements set out under Article 10 of S.I. No. 158 of 2006.

- There are standard operating procedures (SOPs) for the verification of:
  - donor identity
  - details of donor or donor family consent or authorisation
  - assessment of the selection criteria for donors
  - assessment of the laboratory tests required for donors

- There are SOPs describing the procedures for procurement, packaging, labelling and transportation of the tissues and cells to the point of arrival at the tissue establishment or, in case of direct distribution of tissues and cells, to the clinical team responsible for their application or in the case of tissue/-cell samples, to the laboratory for testing.

- Procurement takes place in appropriate facilities, following procedures that minimise bacterial or other contamination of procured tissues and cells.

- Procurement materials and equipment are managed in accordance with the standards and specifications laid down in Directive 2006/17/EC Annex IV ~~section~~Section 1.3 and with due regard to relevant national and international regulation, standards and guidelines covering the sterilisation of medicines, medical devices and surgical instruments.

- Qualified, sterile, single-use instruments and collection devices are used for tissue and cell procurement, unless the use of sterilised reusable instruments is justified.

- Procurement of tissues and cells from living donors takes place in an environment that ensures their health, safety and privacy.

- Where appropriate, the staff and equipment necessary for body reconstruction of deceased donors are provided and such reconstruction is completed effectively.

- The procedures for the procurement of the tissues and cells are carried out in accordance with the requirements of all relevant national and European legislation.

- A unique identifying code is allocated to the donor and the donated tissues and cells, during the procurement or at the tissue establishment, ensuring proper identification of

the donor and traceability of all donated material. The coded data are entered onto a register provided for the purpose. Tissues and cells distributed for human application must have an associated Single European Code (SEC) applied, in accordance with S.I. No. 32 No. of 2019. The SEC means the unique identifier applied to tissues and cells distributed in the European Union and consists of a donation identification sequence and a product identification sequence, and allows for traceability via the EU Coding platform reference compendia.

- Donor documentation is maintained in accordance with ~~point~~Point 1.4 of Annex IV of Directive 2006/17/EC.

- An initial inspection shall be performed by the HPRA of a site following the submission of the relevant application. The HPRA may conduct such additional inspections at establishments/organisations/centres as it considers necessary for the purpose of ensuring compliance with the requirements of legislation. In general, an inspection 12 months after authorisation has been granted, and further inspections every two years thereafter, are performed at a minimum.

- All authorised tissue establishments are required to submit an annual report of their activities to the HPRA. Two report forms have been developed with associated guidance, one for tissue establishments associated with reproductive tissues and cells and the second for all other tissue establishments. The forms and guidance can be found on the HPRA website and should be returned by 31 March each year.

7 PROCUREMENT OF UMBILICAL CORD BLOOD

Under S.I. No. 158 of 2006, it is permissible for a maternity hospital or other institution to apply for an authorisation to procure umbilical cord blood on its premises.

It is also permissible for an organisation, company or person to apply for an authorisation to procure umbilical cord blood at premises other than their own.

In this latter instance, the applicant is required to have a written contract ~~/~~or service level agreement in place with any hospital, clinic or person carrying out the actual act of procurement.

Some hospitals have a policy of not permitting the collection of umbilical cord blood.

However, a staff member may, in their own right, have a contract or service level agreement with a procurement organisation, ~~-~~company or person (who are authorised or have applied

for authorisation to the HPRA) in order to facilitate the collection of umbilical cord blood. This should not affect hospital policy. The relationship between a staff member and the hospital by which he/she is employed is not within the remit of the procurement legislation that is overseen by the HPRA. The HPRA recommends that any staff member who considers entering into such an agreement should discuss the matter with their employer.

A third party may perform the collection of umbilical cord blood on behalf of a procurement organisation, company or person (who are authorised or have applied for authorisation to the HPRA) provided that appropriate service level agreements are in place, the permission of the relevant hospital, clinic or person has been obtained and appropriate training requirements have been met. Medical practitioners or midwives who enter into agreements as outlined above should be aware of the statement issued by the State Claims Agency in September 2008, which is available on their website.

8 REQUIREMENTS FOR THE NOTIFICATION OF SERIOUS ADVERSE REACTIONS AND EVENTS (DIRECTIVE 2015/565/EC)

The HPRA has established a reporting system for the notification of SARs and SAEs. The tissue establishment and/or importing tissue establishment is obliged to notify and provide the HPRA with a report analysing the cause of and ensuing outcome of SARs and SAEs as outlined below, according to the following definitions.

Serious adverse reaction (SAR)

A serious adverse reaction (SAR) is defined as: 'An unintended response, including a communicable disease, in the donor or in the recipient associated with the procurement or human application of tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or prolongs hospitalisation or morbidity'.

Serious adverse event (SAE)

A serious adverse event (SAE) is defined as: 'Any untoward occurrence associated with the procurement, testing, processing, storage or distribution of tissue and cells that might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients or which might result in, or prolong, hospitalisation or morbidity'.

An online reporting form is available under the Report an Issue section of the HPRA website at www.hpra.ie.

Further information in relation to the reporting of SARs and SAEs is available in the 'HPRA Guide to reporting Serious Adverse Reactions and Serious Adverse Events associated with Human Tissues and Cells' or by emailing the HPRA at tissueandcellsafety@hpra.ie.

9 REQUIREMENTS FOR THE IMPORT/EXPORT OF TISSUES AND CELLS FOR HUMAN APPLICATION INVOLVING COUNTRIES OUTSIDE THE EUROPEAN UNION (DIRECTIVE 2015/566/EC)

The import of tissues and cells must be performed by an importing tissue establishment, authorised for this activity by the HPRA. Tissue establishments engaged in the import of tissues or cells on a routine basis from a specific organisation outside the EU are required to have such organisations listed on their tissue establishment authorisation.

Importing tissue establishments must ensure that imported tissues and cells can be traced from donor to recipient, and that such imports meet the standards of quality and safety equivalent to those laid down in EU Directive 2015/566 implementing Directive 2004/23/EC as regards the procedure for verifying the equivalent standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

Establishments who wish to import tissues and cells directly from specific organisation(s) outside the EU can refer to the 'HPRA Guide to Routine Import/Export of Tissues and Cells for Human Application Involving Countries Outside the European Economic Area'.

These documents can be found on the 'Publications and Forms' section of the HPRA website.

~~8~~10 APPLICATION TO THE HPRA FOR AUTHORISATION

As stated above, any entity intending to be involved in the procurement (and ~~also~~ in the testing, processing, preservation, storage, import and distribution) of human tissues or cells intended for human application is required to apply to the HPRA for an authorisation to perform such activities.

All applicants must complete the 'Application for ~~Authorisation of~~ a ~~Tissue Establishment'~~new/importing tissue establishment authorisation' form, which is available on the 'Publications and Forms' section of ~~www.hpra.ie.~~the HPRA website. Further guidance can be obtained by ~~contacting~~emailing the HPRA at compliance@hpra.ie.