

Inspection report on compliance with HTA licensing standards
Inspection date: **8 January 2025**



Arthrex Ltd
Proposed HTA licensing number 22725

Application for a licence under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)

Proposed licensed activities – Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)

‘E’ = Establishment applied to be licensed to carry out this activity and will carry it out.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Arthrex Ltd				E	E	E	

Tissue types applied to be authorised for licensed activities

Applied to be authorised = Establishment to be authorised to carry out this activity and will currently be carrying it out.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Musculoskeletal, Tendon &				Applied to be authorised/	Applied to be authorised/	Applied to be authorised/	

Ligament; Tendon							
Musculoskeletal, Bone; Cancellous Bone Particles				Applied to be authorised/	Applied to be authorised/	Applied to be authorised/	
Skin				Applied to be authorised/	Applied to be authorised/	Applied to be authorised/	
Musculoskeletal, Bone; DBM				Applied to be authorised/	Applied to be authorised/	Applied to be authorised/	
Acellular bone				Applied to be authorised/	Applied to be authorised/	Applied to be authorised/	

Summary of inspection findings

The HTA found the proposed Designated Individual (DI) and the proposed Licence Holder (LH) to be suitable in accordance with the requirements of the legislation.

Although the HTA found that Arthrex Ltd (the establishment) had met the majority of the HTA's standards that were assessed during the inspection, two major (cumulative) shortfalls were found against standards for Governance and Quality, and Premises, Facilities and Equipment, and one minor shortfall against the standards for Disposal.

The HTA has assessed the establishment as suitable to be licensed for the activities specified, subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Compliance with HTA standards

Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) standards

Major Shortfalls

Standard	Assessment Finding	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	The establishment does not have a procedure that describes how non-conforming imported tissues will be managed.	Major (cumulative) <i>The establishment has provided evidence to address GQ1h and GQ2a.</i>
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross-contamination.	The agreement with the proposed courier does not include the requirement to report serious adverse events to the establishment.	
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	The establishment does not have a quality manual.	
GQ2 There is a documented system of quality management and audit.		
a) There is a quality management system which ensures continuous and systematic improvement		

GQ4 There is a systematic and planned approach to the management of records.	<p>There is no documented procedure for record retention in the event the establishment decides to cease licensable activities.</p> <p>The establishment does not have a recall procedure.</p> <p>The establishment's risk assessments are limited in scope and do not cover all intended practices and processes relating to the quality and safety of the tissue.</p>	<p>Major (cumulative – continued from page 4)</p> <p><i>The establishment has provided evidence to address GQ4m, GQ7f and GQ8a.</i></p>
m) In the event of termination of activities of the establishment a contingency plan is in place to ensure raw data and records of traceability are maintained for 10 or 30 years respectively, as required.		
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.		
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall, including notification of the HTA and pre-defined times in which actions must be taken.		

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
a) There are documented risk assessments for all practices and processes.		

PFE1 The premises are fit for purpose.	A risk assessment of the premises has not been undertaken.	Major (cumulative)
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.	The establishment has not yet appointed a nominated, registered medical practitioner and / or a scientific advisor to ensure that the standards laid down by Directions 001/2021 will be met.	<i>The establishment has provided evidence to address PFE1a, PFE1f and PFE4h.</i>
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.	Some of the tissues the establishment proposes to import will have to be stored at -80°C. There is no temperature monitoring procedure in place.	
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.	The establishment's procedure states that frozen allograft will be kept at between -40°C to -80°C for long term storage. The establishment has not defined what is meant by long term storage.	
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.		

d) There is a documented, specified maximum storage period for tissues and / or cells.	<p>The transport box the establishment intends to use to transport decellularized dermis grafts is validated to maintain the temperature below 37°C for 72 hours. However, the recommended storage temperature for decellularized dermis grafts is given as between 15°C and 30°C.</p> <p>The establishment currently has one -80°C freezer. There is no documented procedure that sets out what action should be taken in the event that the freezer fails.</p>	
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.		
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.		
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
k) There are contingency plans for equipment failure.		

Minor shortfall

D1 There is a clear and sensitive policy for disposing of tissues and / or cells.		
a) The disposal policy complies with HTA's Codes of Practice.	<p>The establishment does not have a disposal policy, nor does it provide end users with instructions for the disposal of tissues.</p> <p><i>The establishment has provided evidence to address this shortfall</i></p>	Minor

Advice

The HTA advises the proposed DI to consider the following to further improve practice:

Number	Standard	Advice
	GQ4k	<p>The establishment proposes to hold agreements with hospital trust for the supply of allografts. The agreement informs end users of the requirements to report any serious adverse event or reactions (SAEARs) associated with the allograft and to ensure traceability from donor to recipient are kept for 30 years after the use, expiry or disposal of tissues and / or cells.</p> <p>The DI is advised to consider also providing this information, whenever tissue is distributed, so that the actual end users of the tissues are aware of how to report SAEARs and to ensure that details of the allograft used is documented in the patient notes and the information is retained as required by Directions 001/2021.</p>

Background

The establishment has applied to be licensed for the import, storage and distribution of acellular allografts. An establishment in the United States of America is responsible for the procurement, processing and export of the tissues to an arm of the organisation based in Europe. Arthrex Ltd has applied to import tissues from this third country European supplier.

Description of inspection activities undertaken

The HTA's regulatory requirements are set out in Appendix 1. The following areas were covered during the inspection:

Review of governance documentation

The assessment included a review of the establishment's procedural documentation relevant to the establishment's proposed licensable activities. This included procedures describing the tissue procurer's process for donor assessment, mandatory testing and release of

allografts for export. The assessment also included a review of the establishment's proposed receipt, storage and distribution procedures as well the agreements with the 3CS and the proposed courier that will be used for the distribution of tissues to end users.

Visual inspection

The visit included a visual inspection of the areas where the establishment proposes to undertake the licensable activity. Staff also demonstrated the establishment's temperature monitoring system and management system for receipting and dispatching of material.

Meetings with establishment staff

The assessment included meetings with the following staff: proposed DI, proposed CLH contact, the Product Manager who is also responsible for Quality, Health, Safety, and Environment and representatives of the warehouse and logistics staff.

Report sent to proposed DI for factual accuracy: 22 April 2025

Report returned from proposed DI: 28 April 2025

Final report issued: 15 May 2025

Appendix 1: The HTA's regulatory requirements

The HTA must assure itself that the DI, Licence Holder, premises and practices are suitable.

The statutory duties of the DI are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. The HTA inspects the establishments it licences against four groups of standards:

- consent
- governance and quality systems
- premises facilities and equipment
- disposal.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is given to the proposed DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Appendix 2: Classification of the level of shortfall (HA)

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the Human Tissue Act 2004, Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended), or associated Directions.

1. Critical shortfall:

A shortfall which poses a significant direct risk of causing harm to a recipient patient or to a living donor,

or

A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

A critical shortfall may result in one or more of the following:

- A notice of proposal being issued to revoke the licence;
- Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented;
- A notice of suspension of licensable activities;
- Additional conditions being proposed, or;
- Directions being issued requiring specific action to be taken straightaway.

2. Major shortfall:

A non-critical shortfall.

A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

or

A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

or

A shortfall which indicates a major deviation from the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) or the HTA Directions;

or

A shortfall which indicates a failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

or

A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. Minor shortfall:

A shortfall which cannot be classified as either critical or major and, which can be addressed by further development by the establishment.

This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by

the HTA either by desk based review or at the time of the next inspection.

In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with the final inspection report. Establishments must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection;
- a request for information that shows completion of actions;
- monitoring of the action plan completion, or;
- follow up at next routine site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.

Appendix 3: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

Human Tissue (Quality and Safety for Human Application) Regulations 2007 Standards (as amended)

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.

i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
k) There is a procedure for handling returned products.

l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
n) The establishment ensures imports from third countries meet the standards of quality and safety set out in Directions 001/2021.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 001/2021.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.
GQ2 There is a documented system of quality management and audit.
a) There is a quality management system which ensures continuous and systematic improvement.

b) There is an internal audit system for all licensable activities.

c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.

a) There are clearly documented job descriptions for all staff.

b) There are orientation and induction programmes for new staff.

c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.

d) There is annual documented mandatory training (e.g. health and safety and fire).

e) Personnel are trained in all tasks relevant to their work and their competence is recorded.

f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.

g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.

h) There is a system of staff appraisal.

i) Where appropriate, staff are registered with a professional or statutory body.

j) There are training and reference manuals available.

k) The establishment is sufficiently staffed to carry out its activities.
GQ4 There is a systematic and planned approach to the management of records.
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.

c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
d) There is a system for back-up / recovery in the event of loss of computerised records.
e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) There are procedures to ensure that donor documentation, as specified by Directions 001/2021, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 001/2021.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 001/2021 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.

k) There are documented agreements with end users to ensure they record and store the data required by Directions 001/2021.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan is in place to ensure raw data and records of traceability are maintained for 10 or 30 years respectively, as required.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.

b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.

d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
e) There are procedures to ensure that the premises are secure, and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.

b) There are systems to deal with emergencies on a 24-hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 001/2021.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.

f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions 001/2021.
j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions 001/2021.

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.
a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained.
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.
c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions.
d) New and repaired equipment is validated before use and this is documented.
e) There are documented agreements with maintenance companies.
f) Cleaning, disinfection and sanitation of critical equipment is performed regularly, and this is recorded.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.
i) Staff are aware of how to report an equipment problem.
j) For each critical process, the materials, equipment and personnel are identified and documented.
k) There are contingency plans for equipment failure.

Disposal

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.

c) There is a documented procedure on disposal which ensures that there is no cross contamination.
D2 The reasons for disposal and the methods used are carefully documented.
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.