Site visit inspection report on compliance with HTA licensing standards
Inspection date: **25 February 2020**

Tissue Regenix Ltd.

HTA licensing number 22670

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

Licensable activities carried out by the establishment

Licensed activities

'E' = Establishment is licensed to carry out this activity and is currently carrying it out.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Tissue Regenix Ltd.				E	E	E	

Tissue types authorised for licensed activities

Authorised = Establishment is authorised to carry out this activity and is currently carrying it out.

Authorised* = Establishment is authorised to carry out this activity but is not currently carrying it out.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Musculoskeletal, Bone; DBM				Authorised	Authorised	Authorised	
Musculoskeletal, Bone; Bone				Authorised	Authorised	Authorised	
Musculoskeletal, Tendon & Ligament;				Authorised*	Authorised*	Authorised*	

Tendon							
Membrane, Amniotic; Amniotic Membrane				Authorised*	Authorised*	Authorised*	
Membrane, Fascia Lata; Fascia Lata				Authorised*	Authorised*	Authorised*	

Summary of inspection findings

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

Although the HTA found that Tissue Regenix Ltd. (the establishment) had met the majority of the HTA's standards, four minor shortfalls were found against standards for Governance and Quality.

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.

Minor Shortfalls

Standard	Inspection findings	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.		
n) The establishment ensures imports from non-EEA states meet the standards of quality and safety set out in Directions 002/2018.	The third country supplier's (3CS) documented procedure for donor testing of living donors does not reflect the requirement for blood samples to be collected at the time of donation or, if not possible, within seven days post donation. For example, the 3CS's documented procedure sets out that "specimens will be collected at the time of donation or within seven days prior to or after donation". This allows for an extended period of collection of the samples intended for serology testing. In addition, the 3CS's procedure for screening donors of amniotic membrane does not include an assessment of whether the donor has a history of malignant disease.	**Minor**
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	The third party agreements with the couriers do not include the reporting requirement of serious adverse events and reactions as set out in Directions 002/2018.	**Minor**

GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Internal audits do not cover the full range of activities carried out by the establishment under its licence.	**Minor**

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
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.	The establishment has not set, as a minimum, an annual review of risk assessments for all practices and processes relating to the licensable activities.	**Minor**

The HTA requires the DI to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

Advice

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

Number	Standard	Advice
1.	GQ2 c	In accordance with this licensing standard the establishment is required to conduct an audit in an independent manner at least every two years. The establishment was issued a HTA license less than two years ago and has

		not yet conducted an independent audit. During the inspection the establishment provided assurance that it will be conducting an independent audit in the coming months to ensure compliance with protocols and HTA standards. The DI is advised to review the audit schedule for the independent audit and include the content of what will be audited against all applicable HTA standards. The DI is also advised to document any findings and corrective actions taken. The DI is advised to include horizontal audits of batch processing records for each of the tissue types imported to ensure that the products supplied by the 3CS meet the requirements of the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).
2.	GQ3 k	The establishment is adequately staffed to carry out the licensable activities. However, since the HTA licence was issued there has been a change in the number of staff undertaking the various activities. For example: • only one member of staff is fully trained to release tissue products to end users; and • the call-out phone in case of emergencies is currently the responsibility of a single member of staff, who acts as the initial point of contact. The DI is advised to review the allocation of staff and ensure that there is contingency and succession planning for staff across the different activities.
3.	GQ4 d	The temperature monitoring records are regularly backed-up off-site. Staff at the establishment also perform a weekly, manual back-up of the raw data on the hard drive of a single computer. During the inspection, the data from the hard drive was not readily accessible due to a technical fault on the computer. The DI is advised to consider other options for the back-up of data, such as the shared drive, to ensure it is readily accessible.

		The DI is also advised to document the procedure, as well as any changes introduced, for the back-up and recovery of data.

Background

Tissue Regenix Ltd. (the establishment) has been licensed by the HTA since May 2018. The establishment undertakes the import, storage and distribution of bone, DBM, fascia lata, tendon and amniotic membrane products for allogeneic use. The tissue products are procured, processed and tested for the mandatory serology markers by the 3CS in the United States of America (USA), before they are imported by Tissue Regenix Ltd. The establishment is responsible for ensuring all material imported from the 3CS, stored and distributed to end users comply with all applicable HTA standards.

This was the first site visit inspection of the establishment since the licence application assessment visit (LAAV) inspection, which took place in March 2018. Since the LAAV, there have been no significant changes to the licence arrangements, or the activities carried out under the licence.

Description of inspection activities undertaken

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

Standards assessed against during inspection

There are 121 standards in the Human Application sector of which 87 were assessed. All standards under Consent and GQ5, as well as standards GQ1(e), GQ1(f), GQ1(j), GQ2(d), GQ3(i), GQ4(f), GQ4(g), GQ4(j), GQ8(d), PFE1(d), PFE2(b) and PFE5(g), were not applicable. Standards GQ1(t), GQ3(b), PFE2(c), PFE2(d), PFE4(j), PFE5(d) and PFE5(f) were not assessed.

Review of governance documentation

The inspection team undertook a review of documentation relevant to the establishment's licensable activities. This included procedural documents, including processes related to sample receipt and distribution, records for maintenance of equipment, temperature monitoring for the storage units, agreements, governance meetings, action logs including any incidents and adverse events, audits, risk assessments and staff training records.

Visual inspection
The inspection team undertook a visual inspection of areas where licensable activity is undertaken. This included areas where tissues and cells are received and distributed, the cold storage area and a locked cage for the ambient temperature storage of the tissue products within the warehouse. The establishment is currently not storing any cold chain products.

The designated individual (DI) confirmed that the establishment currently stores relevant material for research under Research Ethics Committee (REC) approval, which is still in date. As such, it was not deemed necessary to inspect the areas where the research material is stored.

Audit of records
Representative records associated with each product were reviewed. These included:

- a traceability audit of a DBM product and a bone product currently in storage and deemed suitable for release to end users;
- a traceability audit of a disposed DBM product;
- a traceability audit of a DBM product and bone product distributed to end users; and
- processing records of two imported products selected prior to the inspection.

Where relevant, the records audited included batch processing records, including donor consent, mandatory serology and sterility testing, and release forms, including certificates of donor eligibility and terminal sterilisation certificates. The inspection team reviewed the processes related to sample receipt and distribution, including the use of the Single European Code (SEC). Also, the electronic database and action log were checked against tissue products that were currently in storage, distributed to end users or disposed of. No discrepancies were noted.

Meetings with establishment staff
Discussions were held with the DI and the person designate (PD) for the establishment. Round table discussions were also held with key staff involved in quality management systems and receipt, storage and distribution of imported tissue products.

Report sent to DI for factual accuracy: 2020.04.02

Report returned from DI: 2020.04.02

Final report issued: 2020.04.02

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 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, 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
   - 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 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
- 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.