Licence application assessment visit report on compliance with HTA licensing standards
Site visit date: **05 February 2020**

Replimune Ltd

Proposed HTA licensing number 12697

Application for a licence under the Human Tissue Act 2004

Activities to be licensed

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose	Removal from the body of a deceased person (otherwise than in the course of an anatomical examination or post-mortem examination) of relevant material of which the body consists or which it contains, for use for a scheduled purpose other than transplantation
Replimune Ltd	To be licensed	Not to be licensed

Summary of visit 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 Replimune Ltd (the 'establishment') had met the majority of the HTA's standards, two minor shortfalls were found against standards for Governance and Quality systems, and Premises, Facilities and Equipment.

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

Minor Shortfalls

Standard	Inspection findings	Level of shortfall
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored		
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.	There are health and safety risk assessments, and risk assessments for the premises and storage facilities, but existing risk assessments do not cover all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.	**Minor**
PFE2 There are appropriate facilities for the storage of bodies and human tissue		
c) Storage conditions are monitored, recorded and acted on when required.	The continuous temperature monitoring system does not cover the -150ºC freezer.	**Minor**

The HTA requires the proposed DI to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfall 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.

Proposed DI and proposed CLH suitability

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

Advice

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

Number	Standard	Advice
1.	N/A	The DI is advised to consider appointing a Person Designated (PD) to assist her in the role. This would be especially important on those occasions when the DI is absent. The HTA must be notified of such an appointment.
2.	T1(c)	The propose DI is advised to consider highlighting freezers that contain human tissue to prevent sample mix-ups, to ensure full traceability and to ensure that staff are aware of the need to manage such samples in line with the regulatory requirements.
3.	PFE1(c)	The proposed DI is advised to consider incorporating periodic decontamination of the -80ºC and -150ºC freezers into the documented cleaning procedure and cleaning schedule to ensure that there is no contamination of stored human tissue.
4.	PFE2(c)	The proposed DI is advised to consider regular challenging of the audible temperature alarms and temperature alarm callout system for the freezers. This will ensure that they are functioning correctly.
5.	PFE2(c)	The proposed DI is advised to consider initiating a programme by which, at suitable intervals, the temperature plots from the monitoring system are reviewed. This may help to identify a potential failure of the system before it occurs.

Background

Replimune Ltd (the ‘establishment’) has applied for an HTA licence. This licence application assessment visit (LAAV) formed part of the application process.

The establishment will store relevant material (peripheral blood mononuclear cells, B lymphocytes, dendritic cells) purchased from HTA-licensed commercial suppliers and used for functional recombinant virus testing.

Description of activities undertaken during visit

The HTA’s regulatory requirements are set out in Appendix 1. The Regulation Manager covered the following areas during the visit:

Standards assessed against during visit

There are 47 standards under the Human Tissue Act 2004 (HT Act). Several standards could not be assessed as the establishment will not directly seek consent, store material from the deceased, have visiting staff or distribute material. Standards which were assessed are set out in Appendix 3 (standards published 3 April 2017).

Review of governance documentation

The following documents were reviewed: policies and procedural documents relating activities to be licensed; temperature monitoring records; contracts for servicing of equipment and records of servicing; agreements.

The review of information related to the quality management system included staff training records and risk assessments.

Visual inspection

The visit included a visual inspection of the area for sample receipt and the storage areas (-80ºC and -150ºC freezers).

Meetings with establishment staff

A roundtable discussion was held with the proposed DI, proposed CLH contact and establishment staff involved with sample receipt and storage. This covered: document control; the management of audits; incidents and risk assessments; contingency and disposal arrangements.

Report sent to proposed DI for factual accuracy: 4 March 2020

Report returned from proposed DI: 17 March 2020

Final report issued: 6 April 2020

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 15 September 2020

Appendix 1: The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the DI is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

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.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

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. They are grouped under four headings:

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

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, 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 provided.

HTA inspection reports are published on the HTA's website.

Appendix 2: Classification of the level of shortfall

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 (HT Act) or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the HT Act or associated Directions

   or

   A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

   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 that:

   - poses a risk to human safety and/or dignity, or

- indicates a failure to carry out satisfactory procedures, or
- indicates a breach of the relevant Codes of Practice, the HT Act and other relevant professional and statutory guidelines, or
- has the potential to become a critical shortfall unless addressed

or

A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

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, but which indicates a departure from expected standards.

   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 site visit.

   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 the proposed action plan establishments 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 Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities. b) There is a document control system. c) There are change control mechanisms for the implementation of new operational procedures.

d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff. e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities. b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training. b) There are documented induction training programmes for new staff. d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records. b) There are provisions for back-up / recovery in the event of loss of records. c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).

GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems. b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. b) Risk assessments are reviewed regularly. c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it. b) A register of donated material and the associated products where relevant, is maintained. c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained;

all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom. d) A system is in place to ensure that traceability of relevant material is maintained during transport. e) Records of transportation and delivery are kept.
T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice. b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose. b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained. c) There are documented cleaning and decontamination procedures.

PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity. c) Storage conditions are monitored, recorded and acted on when required. d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept. b) Users have access to instructions for equipment and are aware of how to report an equipment problem. c) Staff are provided with suitable personal protective equipment.