Licence application assessment report on compliance with HTA licensing standards
Site visit date: **6 May 2022**

Wren Therapeutics Limited

Proposed HTA licensing number 12731

Application for a licence under the Human Tissue Act 2004

Activity 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
Wren Therapeutics Limited	Applied to be licensed	Not applied to be licensed

Summary of assessment 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.

The HTA found that Wren Therapeutics Limited (the 'establishment') had met all of the HTA's standards.

The HTA has assessed the establishment as suitable to be licensed for the activity specified.

Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

Advice

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

Number	Standard	Advice
1.	GQ2(a)	The proposed DI is advised to consider including procedural audits, as well as horizontal and vertical audits, in the establishment's audit schedule to widen the scope of activities that will be subject to review.
2.	T1(c)	There are tissue registers to support the traceability of stored samples. To ensure that they are fully comprehensive, and that the establishment fulfils its obligation as a custodian of the tissue samples, the proposed DI is advised to consider highlighting those samples received from external HTA-licensed Research Tissue Banks (RTBs).
3.	PFE2(c)	The establishment has a continuous temperature monitoring system for its storage units. The proposed DI is advised to consider regular challenging of the temperature alarm callout system and the audible temperature alarms to ensure that they function as expected.
4.	PFE2(c)	The proposed DI is advised to consider initiating a programme by which, at suitable intervals, the temperature plots from the freezer are reviewed. This may help to identify a potential failure of this equipment before it occurs.

Background

Wren Therapeutics Limited ('the establishment') has applied for an HTA licence. The establishment is a drug discovery and development company focused on finding small molecule treatments for protein misfolding diseases (e.g., Alzheimer's and Parkinson's diseases). The establishment will store imported neural tissue and cerebrospinal fluid as well as tissue received from HTA-licensed RTBs.

Description of activities undertaken during the assessment

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

Standards assessed against during the assessment

37 out of 47 HTA licensing standards were covered during the assessment (standards published 3 April 2017). Some standards are not applicable as establishment staff do not directly seek consent [standards C1(a)(b)(d)-(f), C2(a)-(c)], accommodate visiting staff [standard GQ3(c)] or distribute relevant material [T1(g)].

Review of governance documentation

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

The review of information related to the quality management system included: document control; meetings; the management of audits; staff training records; the management of adverse events and complaints; and risk assessments.

Visual inspection

The site visit included a visual inspection of the storage areas (containing two -80ºC freezers).

Meetings with establishment staff

The assessment included a meeting with the following staff: proposed DI, proposed CLH contact and the Human Samples Laboratory Scientist. The meeting covered: consent and disposal; quality management; traceability; and premises, facilities and equipment.

Report sent to proposed DI for factual accuracy: 7 June 2022

Report returned from proposed DI: 15 June 2022

Final report issued: 12 July 2022

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.