Licence application assessment visit report on compliance with HTA licensing standards

Empyrean Therapeutics Ltd.

HTA licensing number 12681

Application for a licence under the Human Tissue Act 2004 for the

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

16 August 2018

Summary of findings

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

Although the HTA found that Empyrean Therapeutics Ltd had met the majority of the HTA's licensing standards, two shortfalls were found against standards relating to Consent and Governance and Quality systems. These related to the agreements with other parties to ensure consent is obtained in accordance with the Human Tissue Act 2004 and the documented system of audits.

The HTA has given the proposed DI advice about SOPs, audits, risk assessments, traceability, courier agreements and storage temperature monitoring.

The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual 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 Designated Individual 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.

Background to the establishment

Empyrean Therapeutics Ltd. (the establishment) is a privately held research and development company working in the field of novel therapeutics for cancer and rare diseases. The establishment collaborates with other companies with similar research interests but no relevant material will be transferred off-site to the collaborators. The establishment has applied for a HTA licence for storage of relevant material, which has come from a human body for use for scheduled purposes. The establishment intends to purchase relevant material from a UK-based commercial supplier for use in their in-house research. The commercial supplier will obtain consent for the relevant material, which will be available to the establishment upon request (see shortfall against C1(c)).

Establishment staff will order relevant material, which includes whole blood and PBMCs from the living, with approval from senior staff. A human tissue tracking form will be prepared in advance of the delivery and a unique 'parent' number will be generated using proprietary software for the incoming sample and a unique 'child' number for each aliquot of T-cells that will be isolated from the original sample. The unique identification codes will track the samples from receipt through to disposal. All cryovials are assigned a unique identification number with their storage location logged in the sample inventory system.

The relevant material will be processed in batches and stored on site. Samples for storage, which are labelled as 'HTA material' - are placed in custom-made, padlocked boxes and kept on a dedicated shelf in a communal -80ºC freezer. The -80ºC storage facility has restricted swipe card access and CCTV. The establishment also has a lockable liquid nitrogen (LN2) dewar with sufficient space to house all relevant material. The LN2 store is also on swipe access control with CCTV. All freezers are on a maintenance contract and serviced annually.

The establishment is renting office and storage space on a purpose-designed research campus in Cambridge. The site provides continuous security to all businesses renting the space and the storage facilities are maintained by the Bioscience Technologies site manager; all of the storage units are connected to a generator back-up facility. The establishment will be monitoring the temperatures of all of their storage units using a wireless data logger. In the event of temperature deviations from acceptable temperature ranges, the storage units will alarm and a mobile alert will be sent to establishment staff, this will keep alerting staff until the until the situation has been addressed. The establishment also have contingency fridge and freezer storage in the event of primary unit storage failure.

The establishment is a new start-up company and at the time of inspection had not performed any work with human tissue. The establishment plans to increase its research activities to include the use of other tissue types for research into drug development in the future.

Description of visit activities undertaken

This report describes a licence application assessment site visit to assess the suitability of the establishment to hold a HTA licence. The suitability of the proposed DI and proposed Licence Holder were assessed. The visit included a review of the establishment's procedures for conducting activities under the licence; meetings with staff; visual inspection of the areas where it is planned that samples will be stored under the licence; and a review of the sample traceability system that will be used.

Visit findings

The HTA found the proposed Licence Holder, the proposed Designated Individual and the premises to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Standard	Inspection findings	Level of shortfall
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the HTA's codes 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.	The establishment did not have an agreement in place with the supplier of the relevant material to ensure that consent would be obtained in accordance with the Human Tissue Act 2004.	**Minor**

GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities	The establishment do not have an audit schedule in place covering licensable activities. The lack of planned audit activities means that there is currently no documented system in place.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1(a)	The proposed DI is advised to ensure that SOPs are prescriptive and detail, step-by-step, the processes involved in updating sample locations on the database. The establishment does not currently have a barcode tracking system due to the small number of samples but the SOP needs to reflect the expected practice for assurance that staff are working to the same practices.
2.	GQ2 (a)	In addressing the shortfall, the proposed DI is advised to audit a representative number of samples when auditing samples in storage for traceability.
3.	GQ6 (a)	The proposed DI is advised to separate the risk assessments so attention can be given to each of the areas of practice requiring compliance with HTA standards.
4.	T1(c)	The proposed DI is advised to consider displaying a sample location map on the freezers where relevant material is being stored to assist with traceability of samples.
5.	T1(e)	The proposed DI is advised to have an agreement in place with couriers transporting samples to the establishment.
6.	PFE2(c)	The proposed DI is advised to ensure that storage temperature monitoring arrangements are documented. This will help to ensure that staff are aware of the temperature monitoring arrangements and the actions to be taken in the event of an alarm. As part of this, the proposed DI is advised to implement regular and formal tests of storage temperature alarms. This will provide assurances that the alarms are functioning as expected and contact the relevant members of staff on the on-call alarm call list. The proposed DI is also advised to ensure that temperature records are monitored for trends. This may help staff to identify when storage conditions may be deteriorating and alert staff to impending equipment failure.

Concluding comments

This report describes the licence application assessment visit of Empyrean Therapeutics, which applied to be licensed under the HT Act for storage of relevant material, which has come from a human body for use for scheduled purposes.

The HTA found the proposed DI and proposed Licence Holder to be suitable. The HTA has assessed the establishment as suitable to be licensed for the activities specified.

Report sent to DI for factual accuracy: 19 September 2018

Report returned from DI: 25 September 2018

Final report issued: 28 September 2018

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: 09 January 2019

Appendix 1: 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.

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
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.
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.
d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
e) Language translations are available when appropriate.
f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
b) Records demonstrate up-to-date staff training.
c) Competency is assessed and maintained.

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.
c) Training provisions include those for visiting 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.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material 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. b) Where relevant, storage arrangements ensure the dignity of the deceased. 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.

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 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 Human Tissue Act 2004 (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:

   (1) A notice of proposal being issued to revoke the licence

   (2) 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.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) 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 CoPs, 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 or 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 both the draft and final inspection report. You 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 desk-based or site-visit inspection.

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