# Licence application assessment visit report on compliance with HTA licensing standards

## Cryosphere Services Ltd

## Proposed HTA licensing number 12688

## 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**

## 8 August 2019

### Summary of visit findings

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

Although the HTA found that Cryosphere Services Ltd (the 'establishment') had met the majority of the HTA's licensing standards, one minor shortfall was found in relation to risk assessments regarding the storage of human tissue.

The HTA has given the proposed DI advice with regards to governance and quality systems, traceability and premises, facilities and equipment.

**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

Cryosphere Services Ltd (the 'establishment') provides specialist storage and logistics management of human biological material, including relevant material, for customers which will include academic institutions, pharmaceutical companies and small to medium sized contract research organisations. The establishment applied for a HTA licence for the storage of relevant material which has come from a human body for use for a scheduled purpose.

The facility consists of a secure cryogenic storage facility containing 14 liquid nitrogen storage tanks, one of which will be used by Cryosphere Services for the storage of human biological material. One tank is currently used to store clinical trial samples, which are exempt from licensing, and will provide contingency storage. Samples will be stored below -175°C in the vapour phase of liquid nitrogen. Secure access to the cryostore is by swipe card only. Material will also be stored within the same premises in two -80°C freezers, one -20°C freezer and at room temperature. All frozen storage units are locked and fitted with audible, automatic alarms which alert a call-out system when temperatures deviate from the set acceptable ranges. All units are subject to an external maintenance schedule and alarm systems are validated and calibrated annually. The room temperature storage unit is also monitored and temperatures are recorded during weekdays.

Relevant material will be stored from both living and deceased donors. Material transfer agreements (MTAs) will be in place with all customers to provide assurance that consent has been given to store relevant material for research. There is a procedure to review the MTAs to ensure that consent has been obtained in accordance with the requirements.

Relevant material will be received, anonymized, from the customer with a pre-labelled unique identification code to track sample receipt, storage, use, transport and disposal. The establishment will use an electronic database to record details to support sample traceability.

## Description of activities undertaken

This report describes a licence application assessment visit to assess the suitability of the establishment to hold a HTA licence. The suitability of the proposed DI, proposed Licence Holder and premises were assessed. The inspection included; 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; 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 | Visit 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. | Although the establishment has a procedure for conducting risk assessments, there are limited documented risk assessments for the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice (see *Advice,* item 2).<br><br>*Prior to the final report being issued the DI submitted evidence of the actions taken in relation to the shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.* | **Minor** |

## Advice

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

| No. | Standard | Advice |
|---|---|---|
| 1. | GQ1(a) | In the *Cryosphere Services Quality Manual*, page 7 (regarding consent), it is stated that tissue from the deceased cannot be stored without consent unless it is for criminal justice or coroner's purposes. The DI is advised to review and amend this to state that tissue from the deceased can be stored and used in research with consent from the deceased person in life, a person nominated by the deceased person or a person in a qualifying relationship with the deceased person (normally a family member). This is in line with the *HTA Code A: Consent* standards and guidance.<br><br>In the document *Controlled destruction of biological samples*, the process to record the reason for disposal is not documented (see *Advice,* item 3). |
| 2. | GQ6(a) | The proposed DI should ensure that documented risk assessments cover all of the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.<br><br>Risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities, including (in this case):<br><br>• receiving and/or storing specimens without appropriate consent documentation;<br>• storing or using human tissue after consent withdrawal;<br>• loss of human tissue;<br>• sample mix-up or loss of traceability;<br>• transport of specimens to and from the establishment; and<br>• incorrect disposal. |

| | | |
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| | | Further guidance on risk assessments of activities conducted under the licence can be found in the HTA's research sector licensing standards and guidance document, which is available on the HTA's website. |
| 3. | T2(b) | The proposed DI is advised to include a separate column in the inventory spreadsheet detailing the reason for the disposal of samples. |
| 4. | PFE2(c) | The proposed DI is advised to implement formal tests of storage temperature alarms and to record that temperature records are monitored for trends. This will help to ensure that the alarms and storage units are functioning as expected. |
| 5. | N/A | The proposed DI is advised to label the freezers that contains human material to increase staff awareness that tissue is being stored in compliance with the Human Tissue Act 2004. |

**Concluding comments**

There is one area of practice that requires improvement, including one minor shortfall.

The HTA requires the proposed Designated Individual 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.

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 proposed DI for factual accuracy: 2 September 2019**

**Report returned from proposed DI: 3 September 2019**

**Final report issued: 3 September 2019**

**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: 11 December 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 |
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| **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 |
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| **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** |
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| 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** |
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| **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 |
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| 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 |
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| **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.