Licence application assessment report on compliance with HTA licensing standards
Assessment date: **10 December 2021**

Crown Biosciences

Proposed HTA licensing number 12725

Application for a licence under the Human Tissue Act 2004

Activities applied 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
Crown Biosciences	Applied to be licensed	N/A

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 Crown Biosciences ('the establishment') was found to have met the most of the standards, three minor shortfalls were identified against HTA standards GQ1(a), GQ2(a) and GQ6(a).

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

Compliance with HTA standards

Minor Shorfalls

Standard	Assessment Findings	Shortfall
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	SOPs do not reflect current practices in sufficient detail to enable staff to carry out activities in a consistent manner.	**Minor**
GQ2 There is a documented system of Audit		
a) There is a documented schedule of audits covering licensable activities	There is no documented audit schedule.	**Minor**
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 no documented risk assessments covering the following: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for useful research; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment ; • security arrangements, and; • incorrect disposal.	**Minor**

Advice

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

Number	Standard	Advice
1.	GQ2(a)	The SOP for HTA audits covers traceability audits only. The proposed DI should consider a wider range of audit activities to demonstrate compliance with our standards and whether the establishment is meeting the requirements of its own systems.
2.	GQ2(a)	The proposed DI, when addressing the shortfall above, should consider the frequency of the audits and audit type to be carried out (e.g. vertical, horizontal, process, observational)

3.	PFE1(c)	There is an SOP in place for the cleaning of laboratory fridges and freezers. The proposed DI is advised to also cover the cleaning of the liquid nitrogen vapour tanks in this SOP, in the event that cleaning and decontamination is required.
4.	PFE2(a)	The proposed DI is advised to consider the potential co-storage arrangements for animal and human tissue, including the appropriate labelling to distinguish between the two. The proposed DI should also have regard to any limitations on the consent that could be relevant to co-storage.
5.	PFE2(c)	The liquid nitrogen vapour tanks and -80 degree Celsius freezers which will hold the relevant material are alarmed and will be subject to continuous temperature monitoring. The proposed DI should consider the placement of signage on the tanks prior to commencing licensed activities, which clarifies and supports the safe storage of human tissue; for example, the alarm set points displayed.

Background

Crown Biosciences (the establishment) was previously licensed by the HTA under licensing number 12598 (2017-19). The licence was revoked as there were no longer any licensable activities taking place.

As the establishment would be resuming licensable activities, with a particular focus on oncology research, they applied to the HTA to be licensed for storage of relevant material for a scheduled purpose under the HT Act 2004. A virtual licence application assessment was carried out in December 2021.

The establishment plans to work with Peripheral Blood Mononuclear Cells (PBMCs) and also Formalin Fixed Paraffin Embedded (FFPE) wax blocks from living donors, obtained from commercial suppliers under agreements to ensure that the requirements of the HT Act 2004 have been met. At the time of the assessment, the establishment did not have any plans to seek consent themselves.

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 assessment:

Standards assessed against during visit

Thirty-nine of the 47 HTA licensing standards were covered during the visit (standards published 3 April 2017). C1(a)(b)(d)(e) and (f) and C2(a) - (c) were not applicable as the establishment staff will not be directly seeking consent.

Review of governance documentation

Key documents were reviewed during the virtual assessment, including but not limited to, the following:

Crown Biosciences Organisational Chart
Quality Manual, version 5 May 2020;
Site Plan
SOP CM28 Operation and Maintenance of Laboratory Fridges and Freezers;
SOP Q7 Internal Audits;
SOP Q9 Document Retention and Achiving Procedure Version 2
SOP HBS Life Cycle Version 2;
SOP HBS 02 Acquisition and Receipt Version 2;
SOP HBS 03 Storage and Usage Version 2;
SOP HBS 04 Transfer and Shipping Version 2;
SOP HBS 5 Disposal Version 2;
SOP HBS 6 Adverse Events and Incident Report and Investigations Version 2;
SOP HBS 07 Performing Risk Assessment for HTA Activities Version 2;
SOP HBS 8 Peforming HTA Audits;

FHBS 06A Adverse Event Incident Report Form, June 2021;
FHBS 07A Human Tissue Sample Risk Assessment Form June 2021;
Risk Assessments Managing Human Biological samples Store Room In Vitro;
RA017 Handling and Use of Human Tissue Samples
RA030 Storage of Human Tissue Samples
Human Tissue Inventory Excel Spreadsheet (Traceability)

Visual inspection

No site visit was undertaken. Establishment staff used a mobile device to facilitate visualisation of the areas where licensable activities would be carried out, which enabled the Regulation Manager conducting the assessment to view the cryostore facility.

Meetings with establishment staff

A roundtable discussion was carried out with the proposed DI, proposed CLHc and proposed Persons Designated (PD).

Report sent to proposed DI for factual accuracy: 24 January 2022

Report returned from proposed DI: 25 January 2022 (no changes)

Final report issued: 26 January 2022

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 Virtual Regulatory Assessment Report.

Date: 10 June 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, and;
- 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, or;
   - 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, or;
- 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.