Site visit inspection report on compliance with HTA licensing standards

Cyprotex Discovery Ltd

HTA licensing number 12653

Licensed 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**

27 June 2018

Summary of inspection findings

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

Although the HTA found that Cyprotex Discovery Ltd (the establishment) had met the majority of the HTA's licensing standards, two minor shortfalls and one major shortfall was found in relation to Governance and quality systems.

The DI has also been given advice on a range of issues.

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

This report refers to licensable activities carried out at Cyprotex Discovery Ltd (the establishment). The establishment is licensed for the storage of relevant material that has come from a human body for use for a scheduled purpose, under the Human Tissue Act 2004 (HT Act). Human samples are stored for use for the scheduled purpose of 'research in connection with disorders, or functioning, of the human body'. The establishment has been licensed since August 2016 and this was the first routine site-visit inspection to assess compliance with the HTA's standards.

Cyprotex Discovery Ltd is located in a multi-tenanted building, which include purpose-designed laboratory facilities. The building and internal doors leading to laboratories have swipe-card controlled access. Samples are stored in a large walk-in -20°C freezer room. The freezer is temperature-controlled and connected to an automated alarm system to alert staff of deviations from the set acceptable temperature ranges, including a call-out notification procedure (see *Advice*, item 7). The freezer works on a dual system that alternates every 4 weeks and automatically switches systems if a system fault is detected. There is also contingency storage space available in an on-site temperature-controlled -80°C freezer.

The establishment is a contract research organisation and acquires samples from external clients. Consent is obtained by the clients and there are agreements in place to assure the establishment that consent procedures comply with the HT Act and the HTA's Codes of Practice. At the time of the inspection, all samples were imported from outside the UK and therefore the consent provisions of the HT Act do not apply. Samples are sent to the establishment using tracked couriers. All relevant material has a unique identification code which is used to track sample receipt/collection, storage, use, transport off site and disposal. The establishment uses paper records to record details of sample traceability; however, there are plans to implement a LIMS system in the future (see *Advice*, item 4).

There are overarching governance documents that cover all main activities being carried out under the licence. Some projects have approval from recognised research ethics committees (RECs) and are exempt from the licensing requirements of the HT Act; however, the establishment adopts a harmonised approach to governance and sample management.

Description of inspection activities undertaken

The inspection timetable was developed in consideration of the activities conducted under the licence, compliance update information, discussions with the DI, previous communications with the HTA and the findings of the previous inspection. The inspection included review of the establishment's procedures for conducting activities under the licence and roundtable discussions with the DI and CLHc. The inspection also included a visual inspection of the laboratory areas where licensable activities take place. The following audits were performed:

- Five samples, from paper records to sample storage.
- Three samples, from storage to paper records.
- Disposal records for a completed study.

All samples were fully traceable and no anomalies were found.

Compliance with HTA standards

Standard	Inspection findings	Level of 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.	The establishment works as a contract research organisation and agreements are in place with a number of clients; however, information relating to the samples lacks detail. For example, samples are stored for REC-approved projects; however, the establishment does not know the expiry dates of the REC approvals and so are unaware of when the samples would fall under the licence. As a result, samples have been sent from the establishment to unlicensed premises and have been stored in breach of the HT Act.	**Major**
GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	Audits are undertaken at the establishment; however, licensed activities are not currently included. *Refer to Advice, item 2.*	**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.	Although the establishment has a procedure for conducting risk assessments, there are no documented risk assessments of the risks associated with the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. *Refer to Advice, item 3.*	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1(d)	There are regular meetings between the DI and CLHc where governance matters relating to licensed activities are discussed. The DI is advised to formalise these meetings and minute them. Documented minutes should be

		distributed to all relevant staff to help to ensure that they are aware of all important information relating to licensed activities at the establishment.
2.	GQ2(a)	Audits are undertaken at the establishment; however, licensed activities are not currently included. To address the minor shortfall against standard GQ2(a), the DI is advised to create a schedule of audits to demonstrate compliance against the HTA standards. Vertical audits of records and samples should allow the establishment to assure itself that samples and records are fully traceable from consent to use or disposal. Audits should ideally include horizontal audits by staff involved in the processes, to ensure that SOPs accurately reflect actual practices and to identify areas for improvement. Audits should be carried out on a periodic basis, or following a change in process. The DI is advised that audit findings and corrective and preventative actions should be recorded, and should include timeframes for completion. The DI may wish to develop a form to record audits so that they are consistently captured and followed-up.
3.	GQ6(a)	To address the minor shortfall against standard GQ6(a), the 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. In particular, the proposed DI should ensure that the following risks have been assessed: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • loss of human tissue; • sample loss of traceability; • transport of specimens to and from the establishment; and • incorrect disposal. 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.
4.	T1(b)	The DI is advised to review the sample tracking process and advance plans to implement an electronic system for routine sample tracking.
5.	T1(c)	Paper records detail the storage location of samples, indicating the freezer tray. The DI is advised to specify the actual location of each sample within the freezer tray to strengthen sample traceablilty. Furthermore, the storage boxes containing relevant material do not have suitably fitted lids. The DI is advised to use more secure boxes to prevent sample loss.
6.	T2(a)	There is a thorough record of samples that have been disposed of which detail the method, reason and date of disposal. This procedure, however, is not documented in the disposal SOP. The DI is advised to update *SOPG009*.
7.	PFE2(c)	Temperatures of all freezers should be assessed frequently to identify any trends that may herald impending equipment failure. All relevant material is stored in freezers that have external alarm and call-out systems. The DI is advised to establish a system of regular manual challenge of the alarm systems to ensure that, when temperature deviations are detected, the system operates successfully.

		The DI is advised to keep the contingency freezer under regular maintainance.
8.	PFE3(a)	The building's Estates Department manages servicing and maintenance of the facilities and equipment. The DI is advised to ensure that the establishment receives copies of servicing and maintenance records. This will help staff to ensure that maintenance schedules are appropriate and that they are made aware of any issues which may impact on operational matters.
9.	N/A	The DI is advised to consider appointing a PD to assist them in their role.

Concluding comments

This report outlines the first routine inspection of the establishment.

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

Although the HTA found that the establishment had met the majority of the HTA's standards, two minor shortfalls and one major shortfall was found in relation to the Governance and quality systems standard.

The HTA requires the Designated Individual to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls 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 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.

Report sent to DI for factual accuracy: 24 July 2018

Report returned from DI: 24 July 2018

Final report issued: 08 August 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: 23 November 2018

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.