Site visit inspection report on compliance with HTA licensing standards
Inspection date: **13-14 November 2019**

Clinical Trial Service Unit and Epidemiological Studies Unit

HTA licensing number 12168

Licensed under the Human Tissue Act 2004

Licensed activities

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
Hub site **Clinical Trial Service Unit and Epidemiological Studies Unit**	Licensed	Not licensed
Satellite site **Unit 17 Wornal Park**	Licensed	Not licensed

Summary of inspection findings

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

Although the HTA found that the Clinical Trial Service Unit and Epidemiological Studies Unit ('the establishment') had met the majority of the HTA's standards, one minor shortfall was found against a standard for Governance and Quality systems.

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 shortfall identified during the inspection.

Compliance with HTA standards

Minor Shortfall

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.	There are inconsistencies between the hub and satellite documents concerning sample management. The hub procedure includes the management of non-conforming samples received into the establishment but the satellite procedure does not.	**Minor**

The HTA requires the DI 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.

DI and CLH suitability

The HTA found the Designated Individual (DI) and the Corporate Licence Holder (CLH) to be suitable in accordance with the requirements of the legislation.

Advice

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

Number	Standard	Advice
1.	C1(a)	The procedure for seeking consent for non-study samples does not include the option of withdrawal of consent, although this option is included on the consent forms. The DI is advised to consider adding this option to the procedure to ensure consistency.
2.	GQ1(a)	The establishment is also accredited under ISO 17025: 2017. The Quality Manual is written against the ISO 17025: 2017 standards. The DI is advised to consider providing a similar document written against the HTA standards or to add references to the HTA standards; for example, as an Appendix.
3.	T2(b)	The establishment follows the University's policy on incineration when disposing of samples. The DI is advised to reference this method of disposal in the local procedure.
4.	PFE1(c)	The DI is advised to consider incorporating periodic decontamination of the -40ºC and 80ºC freezers into the documented cleaning procedure and cleaning schedule.
5.	PFE2(c)	The DI is advised to consider additional testing of the temperature alarm callout system to provide further assurance that it is functioning correctly.

6.	PFE2(c)	The DI is advised to consider initiating a programme by which, at suitable timeframes, the temperature plots from the monitoring system are reviewed. This may help to identify a potential failure of the system before it occurs.
7.	PFE2(d)	There are detailed documented contingency plans for off-site storage at an HTA-licensed establishment. The DI is advised to consider including a similar level of detail in the local plans for the use of alternative freezers and the use of the satellite facilities to ensure that all members of staff can follow such plans swiftly and effectively.

Background

The Clinical Trial Service Unit and Epidemiological Studies Unit (the establishment) has been licensed by the HTA since May 2008. This was the second site visit inspection of the establishment; the last inspection took place in March 2009.

The establishment is part of the Nuffield Department of Population Health (NDPH) within the University of Oxford. It provides scientific and diagnostic support for large-scale observational studies and randomised trials. The establishment stores relevant material (adipose and cardiac tissue, urine, buffy coat, whole blood) and non-relevant material (plasma, serum). At the time of the inspection, relevant material from 18 studies was being stored. Five of these (170,000 samples) have current UK Ethics Committee Authority (UKECA) approval and the storage of these samples is exempted from HTA licensing. The remaining 13 licensed studies (430,000 samples) have University of Oxford ethical approval or the UKECA approval has expired. Additionally, urine and blood samples have been obtained and stored from patients and healthy volunteers (4,400 samples) for biomarker validation research under current NHS project-specific Research Ethics Committee (REC) approval ('non-study' samples). Consent for non-study samples is sought by trained staff within the establishment or is sought within the adjacent Trust under agreement.

Since the previous inspection, the following changes have been made to the licence arrangements: the current DI was appointed in May 2010; the current CLH contact (CLHc) was appointed in October 2018; and a satellite licence was revoked in December 2015 at the request of the DI. The material previously stored under this satellite licence is now stored at a separate HTA-licensed establishment, under a service level agreement. The establishment also uses this other establishment as a contingency storage.

Description of inspection activities undertaken

The HTA's regulatory requirements are set out in Appendix 1. The inspection team covered the following areas during the inspection:

Standards assessed against during inspection

Standard PFE2(b) was not applicable to the inspection. All remaining 46 licensing standards were covered during the inspection (standards published 3 April 2017).

Review of governance documentation

The following documents were reviewed: policies and procedural documents relating to licensed activities; meeting minutes; audits; staff training records; reported incidents; risk assessments; temperature monitoring of the storage units; contracts for servicing of equipment and records of servicing; and agreements (service agreements, material transfer agreements).

Visual inspection

The inspection included a visual inspection of both the hub and satellite sites. Areas inspected at each site were the those for sample receipt and release as well as the storage areas (hub storage: -40ºC and 80ºC freezers; satellite storage: liquid nitrogen tanks).

Audit of records

Traceability audits were performed on 27 stored samples (hub: six samples, from three separate studies, and two non-study samples; satellite: 19 samples, from three separate studies). The samples were selected at random from each storage facility and the labelling, date of receipt and storage location details were compared to the electronic records. There were no discrepancies noted.

As consent is sought elsewhere, evidence of consent was accepted if an up-to-date agreement was available with the relevant collecting organisation and copies of the template consent form and participant information sheet were available. For the two non-study samples, the

consent obtained was completely unlinked from the donor's details so copies of the template consent form and participant information sheet were also accepted as evidence. There were no discrepancies noted.

Meetings with establishment staff

Roundtable discussions were held with relevant staff working under the licence at both sites covering: the management of audits; incidents and risk assessments; governance meetings and training; standard operating procedures (SOPs); document control; contingency arrangements; agreements; distribution; and disposal. Further discussions were held with staff involved in seeking consent, and with the Persons Designated. Individual interviews were held separately with the DI and the CLH contact.

Report sent to DI for factual accuracy: 10 December 2019

Report returned from DI: 18 December 2019

Final report issued: 16 January 2020

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.