Site visit inspection report on compliance with HTA licensing standards

The Francis Crick institute

HTA licensing number 12650

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**

5 March 2019

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 The Francis Crick Institute had met the majority of the HTA's standards, one minor shortfall was found against one Governance and quality systems standard. This was in relation to the absence of regular governance meetings, where matters relating to HTA-licensed activities could be discussed.

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

The Francis Crick Institute is a new, state-of-the-art-building, which opened in 2016, and is located in central London. It is the biggest biomedical research facility under a single roof in Europe. The Institute is an independent organisation funded by the Medical Research Council (MRC), Cancer Research UK, Wellcome, UCL, Imperial College and King's College London.

There are two founding institutes that combined researchers to form The Francis Crick Institute ('the establishment'): the MRC-funded National Institute for Medical Research (NIMR) at Mill Hill, London; and The Clare Hall Laboratories, funded by Cancer Research UK, in Hertfordshire. The Institute is currently occupied by 1800 researchers and support staff, and can accommodate up to 2000 people. On three research levels, it is divided into quadrants (NW, NE, SW & SE), with an assigned manager for each quadrant; the fourth research level only has two quadrant managers. There are currently no 'Persons Designated' (PDs) on the licence; it is intended that all quadrant managers will be formally added to the licence as PDs following the completion of the inspection process.

The establishment uses human tissue from a number of sources: imported tissues from commercial companies; imported tissue from collaborative overseas research projects (i.e. Europe and Africa); internal (anonymised) healthy blood donations; and surplus anonymised blood from NHSBT. It is an institutional policy that imported tissue will only be accepted when it is accompanied by an Material Transfer Agreement (MTA). The consent requirements of the Human Tissue 2004 (HT Act) do not apply to these imported samples; however, the researchers receiving human tissue from overseas projects, are often involved in designing the consent forms. In addition, staff actively request consent templates when purchasing relevant material from commercial sources.

Consent for healthy volunteers is sought only by the CLHc and the DI, and a donor log is kept to monitor donations. Researchers wanting to use anonymised volunteer blood donations are not permitted to collect directly from the donation suite; blood donations are delivered directly to the laboratories. It is institutional policy that healthy blood donors are not permitted to donate to their own research projects. A generic request for blood donations is sent throughthe weekly email bulletin called 'Friday round up'; there is also an internal user group for researchers wishing to use internal blood samples.

The establishment also stores human tissue for specific research projects that have received ethical approvals from NHS Research Ethic Committees (RECs), meaning that tissue storage is exempted from the licensing requirements of the HT Act. Advice was given to the establishment in relation to the tracking of end of project dates for these REC approved studies (see *Advice*, item 6).

There are a large number of research groups using human tissue samples under HTA licence. These groups conduct basic biological research to understand disease development and translate this to help prevent, diagnose and treat a range of different diseases. The tissue samples are stored under room temperature (RT), -80°C freezer and liquid nitrogen (cryostore) conditions.

This is the first routine inspection at The Francis Crick Institute since their licence was granted in 2016. A previous inspection was conducted in 2015 at The Francis Crick at Mill Hill under a previous licence (HTA licensing number 12272). All human tissue samples held under licence at Mill Hill (12272) were transferred to The Francis Crick Institute under their new licence (HTA licensing number 12650).

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 and previous communications with the HTA. The inspection included a review of the establishment's procedures for conducting activities under the licence and interviews with staff involved in consent seeking, quality management and sample management. The inspection also included a visual inspection of the areas where samples are stored under licence and audits of sample traceability. Audits of the following, randomly-selected samples were conducted, covering all storage locations:

- Two samples from -80°C freezer storage, comprising of anonymised human peripheral blood mononuclear cells (PBMCs) from staff donors, traced to consent and sample tracking system.
- Four samples (human keratinocytes) from cryostore, to receipt from commercial supplier and consent template.
- Two samples (human spleen cell suspension) from cryostore to receipt of imported cells from collaborator, to sample tracking system and the consent template.
- One slide and one wax block (human cerebellum), at RT, to sample tracking system.

All samples were fully traceable

Inspection findings

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

Compliance with HTA standards

Governance and Quality systems

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		
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.	The 'Human Ethics Group (HEG)' at The Francis Crick Institute assesses the ethical considerations and risks of research project proposals for those researchers wishing to access human biological samples (whole blood, PBMCs) from staff healthy volunteers. The HEG meets only once each year and it is the only platform where HTA-related activities and HT legislation are discussed. See also *Advice*, item 3	**Minor**

Advice

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

No.	Standard	Advice
1.	C2(b)	There is evidence to demonstrate up-to-date staff training for all HTA-related activities. The DI is advised to introduce refresher training for staff involved in HTA-licensed activities, at appropriate time intervals.
2.	GQ1(c)	The DI is advised to ensure the distribution of Institute SOPs and risk assessments for all HTA-licensed activities to relevant staff. In addition, the DI is advised to document that relevant staff have read the SOPs and this is documented in their training records.

3.	GQ2(a)	There is potential for HTA-licensable activities to increase amongst existing research groups and it was noted that space is available in the Institute to recruit new research groups. The DI is advised to consider how auditing can be maintained as a useful tool in the future. For example, the Persons Designated (PDs) could play a key role in auditing. Additionally, the DI may like to consider extending the range of audits undertaken as part of the audit schedule, involving different members of staff.
4.	GQ3(b)	The DI may wish to consider introducing a brief 'HTA awareness' to all Institute Laboratory inductions.
5.	GQ5(a)	Although there is a system for the reporting of adverse events to human tissue held under HTA licence, not all of the staff involved in HTA-licensed activities were aware of how to do it. The DI is advised to review and strengthen staff training to raise awareness on the identification and reporting of adverse events.
6.	T1(c)	Although there is one main system used by a number of research groups to track their samples, relevant material held under the HTA licence is tracked on a number of different systems. During the inspection, the DI explained that it is the intention that all samples will be held by one main sample tracking system to allow greater oversight of all relevant material held under licence by all the research groups. The DI is encouraged to procede with this work and is advised to add all tissue samples held under specific, REC-approved projects onto the main sample tracking system, including the expiry dates of the REC approvals. This may help the DI to have oversight of these samples if they are subsequently stored under the HTA licence.
7.	T1(c)	To raise awareness and facility traceability, the DI is advised to add external signs to all equipment where human samples are stored under licence.

Concluding comments

The majority of the HTA licensing standards were met, with one minor shortfall found in relation to governance and meetings. Advice has also been given to the establishment on a range of matters.

The HTA requires the 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 time frames with 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 / subject to compliance with the additional conditions applied to the licence.]

Report sent to DI for factual accuracy: 01 April 2019

Report returned from DI: 09 April 2019

Final report issued: 09 April 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: 01 May 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.