Licence application assessment visit report on compliance with HTA licensing standards

Affinity Biomarker Labs

HTA reference number 12689

Application to be 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**

23 April 2019

Summary of inspection 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.

While Affinity Biomarker Labs Limited was found to have met the majority of the HTA standards five minor shortfalls were found against the Governance and quality systems, Traceability and Premises, facilities and equipment standards.

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 (HT Act). 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

Affinity Biomarker Labs (the 'establishment') is a privately held, Contract Research Organisation (CRO) that has applied for a HTA licence to store relevant material which has come from a human body for use for scheduled purposes. The establishment provides a bespoke analytical service to assist in the discovery, verification, validation and analysis of novel, esoteric, biomarkers in a diverse range of human samples. To date the establishment have received serum, plasma, cerebral spinal fluid (CSF) and saliva for analysis. The establishment does receive whole blood for analysis, but these samples are processed immediately upon receipt and no licensable storage takes place.

The establishment receives material for analysis from customers engaged in clinical, developmental and academic research. Currently, all material is received from groups within the UK although the establishment expects to expand their customer base globally. All material received to date has been collected under approval from a recognised Research Ethics Committee (REC), or in the case of several of the academic studies, with approval from a local University REC. Material stored under approval from a recognised REC is exempted from the licensing requirements of the Human Tissue Act 2004. This exemption does not extend to material stored under the auspices of a University REC, and any relevant material from these studies must be stored under the HTA licence.

The establishment is notified in advance of sample shipment and ensure that staff are in place to receive the material. Shipments are unpacked in an access-controlled laboratory, the samples visually checked and the number and details of boxes recorded in an online spreadsheet. Samples are provided in pre-defined boxes for sample analysis and, to preserve sample integrity, staff do not confirm the identity of each sample vial, although the total number of vials is confirmed. All shipments are accompanied by box maps providing individual IDs for all samples within each box. The batch records for the shipment are countersigned by establishment staff and a receipt acknowledgement returned to the shipping establishment. The boxes are transferred to an alarmed and monitored -25°C freezer for storage until analysis. Currently, the establishment does not store any material once it has completed analysis, with all material either being used to destruction during analysis or any residual material either being disposed of or returned to the customer.

The establishment logs all studies into a spreadsheet and links each study to a copy of the relevant REC approval letter for that study (see *Advice*, item 3). Individual spreadsheets are developed for each study in order to track individual samples while they are stored at the establishment.

At the time of the site visit, contingency planning involved material being stored in neighbouring laboratories in the event of equipment failure (see shortfall against PFE2(d)).

Description of site visit activities undertaken

This report describes a licence application assessment site visit to assess the suitability of the establishment to hold a HTA licence. The suitability of the proposed DI and the proposed Corporate Licence Holder contact (CLHc) were also assessed. The inspection included a review of the establishment's procedures for conducting activities under the licence, a visual inspection of the areas where samples will be stored under the licence, and interviews with the proposed DI and the proposed CLHc.

At the time of inspection, the establishment were not storing any relevant material that would require a HTA licence to be in place. Historical records for samples that had been received by the establishment were reviewed. All relevant material received prior to the inspection was covered by recognised REC approval, and the only material received by the establishment under local REC approval was serum. The sample traceability spreadsheets and documentation (sample receipt, ethical approval letter, sample disposal form etc.) associated with two shipments of samples were reviewed. One shipment comprised 1485 samples from 2017 and the other comprised 1355 samples from 2019. It was noted that the sample disposal form did not record the reason for disposal (see shortfall against T2(b)). No other anomalies were found.

Inspection findings

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

Compliance with HTA standards

There were five minor shortfalls identified against the HTA standards.

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	At the time of inspection, the establishment's schedule of audits did not include an audit of consent or ethical approval status for the samples received.	**Minor**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills		
d) Staff have appraisals and personal development plans.	The establishment does not currently have appraisal and personal development plans.	**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.	The establishment risk assessments do not include all of the risks relating to the premises, practices and procedures connected with licensed activities. Examples of areas not currently covered include risks associated with: - 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; - loss of human tissue; - sample mix-up or loss of traceability; - transport of specimens to and from the establishment ; - security arrangements; - incorrect disposal.	**Minor**

Traceability

Standard	Inspection findings	Level of shortfall
T2 Bodies and human tissue are disposed of in an appropriate manner		
b) The date, reason for disposal and the method used are documented.	While the establishment records the date and method of disposal for relevant material, they do not currently record the reason for disposal.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE2 There are appropriate facilities for the storage of bodies and human tissue		
d) There are documented contingency plans in place in case of failure in storage area.	The establishment stores relevant material in a -25°C freezer. In the event of freezer failure, the establishment will temporarily store material in freezer units in adjacent laboratories. This arrangement has not been documented.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ2(a)	In addition to vertical audits, the proposed DI is advised to consider adding horizontal audits to the schedule. These audits should ideally be undertaken by staff involved in the processes and would ensure that SOPs accurately reflect actual practices and identify areas for improvement.
2.	GQ3(b)	The proposed DI is advised to consider making specific training in the requirements of the Human Tissue Act 2004 available to staff. This training could be developed in house, or the establishment could utilise one of the training systems available externally and online.
3.	T1(c)	While the establishment determines if material was collected under approval from a recognised REC, the proposed DI is advised to confirm and record the end dates of approvals to ensure that material may be moved to the governance of the HTA licence should it be required.

Concluding comments

This report describes the licence application assessment visit to determine the suitability of the establishment to be licensed under the HT Act 2004 for storage of relevant material which has come from a human body for use for scheduled purposes.

While the establishment has met the majority of the HTA standards, there are a number of areas of practice that require improvement, including five minor shortfalls that have been identified against the HTA standards.

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 assessment visit.

Report sent to DI for factual accuracy: 28 May 2019

Report returned from DI: No factual accuracy or request for redaction comments were made by the DI.

Final report issued: 13 June 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: 15 July 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
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.

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.