Site visit inspection report on compliance with HTA licensing standards

Eurofins Pharma Bioanalysis Services UK Limited

HTA licensing number 12572

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**

10 October 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.

The HTA found that, although Eurofins Pharma Bioanalysis Services UK Limited (the establishment) had met the majority of the HTA's licensing standards, four minor shortfalls were identified relating to the Consent, Governance and Quality systems and Traceability standards.

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 Eurofins Pharma Bioanalysis Services UK Limited (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 September 2010 and this was the second routine site-visit inspection to assess whether it continued to meet the HTA's standards.

The establishment is a Contract Research Organisation (CRO) providing bioanalytical services at all stages of drug development to external clients. Relevant material is obtained from clients, collected in-house or purchased from commercial suppliers. Samples are mainly processed blood components including plasma, serum and peripheral blood mononuclear cells (PBMCs). Many of the human samples stored for research are part of clinical trials and are held under clinical trial (UKECA) approvals. Although these are exempted from the licensing requirements of the HT Act, there is overarching and harmonised governance of all collections.

Fresh blood samples are obtained in-house to use in assay development. The project lead is responsible for seeking consent from members of staff (see *Advice*, item 5). Consent is sought using a project-specific consent form and an accompanying information sheet (see *Advice*, items 3 and 4). Although details of the consent seeking process is documented, consent seekers do not receive specific training that addresses the requirements of the HT Act and the HTA's Codes of Practice (see shortfall against C2(a)). Once consent is sought, samples are obtained from the donors by a state registered phlebotomist. Samples are deidentified and coded before being transferred into the laboratory.

For study samples, consent is obtained by the clients and there are master service agreements in place. Many samples sent from external clients are 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 and are stored on site until completion of the project, after which they are disposed of, sent back to the client or retained if requested (see shortfall against T2(a)).

The establishment is located in a multi-tenanted building with access to the building and to the laboratories restricted to authorised personnel only. Visitors must be accompanied and are required to sign in and out at the entrance. Some samples are stored in a 'working' freezer in the main laboratory; however, the majority of the samples are stored in a designated sample management room. This room is further secured and access is restricted to key members of staff and the sample management team. The team are responsible for the traceability of all of the samples. Upon arrival the team check samples against the manifests,

locate storage areas and records details on an electronic sample management tracking system. Analysts wishing to use any samples fill out a request form and staff from sample management locate them, record the details and sign them out.

Samples are stored in freezers or in liquid nitrogen tanks (see *Advice,* item 11). The freezers are fitted with automated alarms that are triggered by deviations from the set acceptable temperature ranges. If temperatures go out of range, an external monitoring service alerts relevant members of staff by telephone, 24 hours a day and, in the event of a power failure, they are connected to the emergency supply. The alarm systems are routinely tested and trends are reviewed. Freezers are maintained and are subject to servicing. There is one liquid nitrogen tank within the sample management room that is also connected to an external monitoring alarm system. Samples are stored in the vapour phase and there is a contracted company that maintains liquid nitrogen levels weekly; they are also on-call if a problem arises. The establishment informed the HTA that they are currently in the process of getting another liquid nitrogen tank for contingency (see *Advice*, item 12).

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 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 the licence and audits of sample traceability. Audits of the following, randomly-selected samples were conducted:

- Fourteen samples from frozen storage to evidence of consent.
- Two disposal records.

For the samples audited, vials were labelled with single numbers only. Not every vial had a unique reference number, which is not in accordance with the establishment's SOP. The box containing the samples had multiple study numbers on and the number of vials listed on the box was incorrect (see shortfall against T1(a)).

Inspection findings

Compliance with HTA standards

Standard	Inspection findings	Level of shortfall
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.	Although details of the consent seeking process is documented, consent seekers do not receive specific training that addresses the requirements of the HT Act and the HTA's Codes of Practice.	**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 does not have any risk assessments relating to licensable activity.	**Minor**
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.	Although the SOP for the 'Collection and Storage of Human Tissue from Volunteers' states that samples should be given a unique identification code containing the donor sample, year and sequential number, this procedure is not being followed. Samples found on the traceability audit were labelled with single numbers only.	**Minor**
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.	The disposal spreadsheet identified a backlog of samples that have been marked as 'to be disposed of'; however, this has not yet been carried out. Although there is no risk that these samples will be used for research, and it is clear that they are for disposal, some samples have been held for disposal for more than one year. Furthermore, when projects are finished and closed, the establishment does not have a robust procedure for the timely disposal of samples.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1(a)	Donor thresholds have been established but they are not monitored. The DI is advised to monitor donation quantities, such that donors do not donate excessively.
2.	C1(a)	The establishment approaches staff members during the induction process to discuss donating blood. The DI is advised to implement a cooling off period whereby staff are at the establishment for a period of time before donation is discussed.
3.	C1(b)	It is advised that the consent forms and information sheets reference the HT Act.
4.	C1(b)	Although the consent form explains to the donor that consent may be withdrawn at any time, it does not explain the process of how to withdraw consent. The DI is advised to add this information.
5.	C1(b)	The consent forms do not record the consent seekers name, although this can be traced back to the project lead. The DI is advised to add this information to the form, including space for the consent seeker to sign and date so that it is more robustly evidenced.
6.	GQ1(a)	The SOP BAL-212 for the 'Collection and Storage of Human Tissue from Volunteers' states that 'a licence to store tissues for diagnostic and research/scientific purposes was granted under the Human Tissue Act 2004'. Diagnosis is not a scheduled purpose under the Act and therefore this should be corrected.
7.	GQ1(a)	The process to follow if a donor were to withdraw consent needs to be documented within the relevant SOP.
8.	GQ1(d)	Although staff discuss HTA matters at relevant meetings, the DI is advised to add this as a standing agenda item.
9.	GQ3(b)	Staff have annual appraisals and personal development plans, although this has not been carried out this year. The DI is advised to schedule this annually so it is not overlooked.
10.	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 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.
11.	PFE2(b)	None of the freezers containing relevant material are labelled. The DI is advised to label every freezer that contains human material to increase staff awareness.
12.	PFE2(d)	The DI is advised to formally agree a contingency storage failure for the liquid nitrogen tank.
13.	N/A	The DI is advised to make staff aware of the HTA's bi-monthly newsletter, which may help them to keep abreast of relevant information for the areas they work in.

Concluding comments

This report outlines the second 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, four minor shortfalls were found in relation to the Consent and Traceability 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 inspection.

Report sent to DI for factual accuracy: 05 November 2018

Report returned from DI: 15 November 2018

Final report issued: 16 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.