Site visit inspection report on compliance with HTA minimum standards

F-Star Biotechnology

HTA licensing number 12622

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**

17 June 2015

Summary of inspection findings

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

Although the HTA found that F-Star Biotechnology (the establishment) had met the majority of the HTA standards, one major and five minor shortfalls were found, in relation to Governance and Quality systems (GQS), Premises, Facilities and Equipment (PFE) and Disposal (D) standards. The shortfalls were in relation to the development of the overarching governance documents, document control procedures, audit and risk assessments of both the premises and the practices; and disposal of relevant material. Advice has also been given relating to other Consent (C), GQS, PFE and D standards.

Particular examples of good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, Licence Holder, premises and practices are suitable.

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.

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. The HTA inspects the establishments it licenses against four groups of standards:

- consent
- governance and quality systems
- premises facilities and equipment
- disposal.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, 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 given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

F-Star Biotechnology (the establishment) is a research organisation specialising in developing novel bispecific antibody products. The establishment is licensed under the Human Tissue Act 2004 (the HT Act) for the storage of relevant material for use for scheduled purposes.

This report describes the first site visit inspection of the establishment since it was issued an HTA licence in August 2014. The establishment stores Peripheral Blood Mononuclear Cells (PBMCs) extracted from leukocyte cones for use in research. The establishment also stores PBMCs which have been expanded and do not contain original human cells, thereby exempting storage of these samples from the HT Act licensing requirements.

The establishment receives anonymised leukocyte cones from NHSBT. The establishment has a documented agreement with the supplier. The HTA has given advice to the Designated Individual (DI) to further strengthen the establishment's assurance that consent for the use of samples for research is in accordance with the legislative requirements (see advice item 1).

The leukocyte cones are transported by a member of staff from the hospital to the establishment. The premises are secure and there is a key card access to enter the building and to enter each floor. PBMCs are extracted in a dedicated lab, aliquoted and stored in a -150 ^{0}C freezer located in a storage room. All human samples are stored separately to non-human samples. The freezer is not locked and is kept in a storage room shared by other companies based within the same building (see advice items 10 &11). The freezer is continually temperature-monitored and there is a local alarm (see advice items 12 & 13). The freezer is monitored by members of staff during the day and campus security visits the storage room every hour, out-of-hours. The freezer has labels which display contact information of the responsible persons to be contacted in the event of a deviation from the set acceptable ranges. The establishment has contingency arrangements for storage in the event of equipment failure.

All PBMC aliquots from a single donor are assigned the same alphanumeric unique identifier code. The establishment uses an electronic database to provide traceability of samples. Sample traceability is managed by all staff who use human tissue samples. The database is updated when an aliquot is removed by a member of staff. From May 2015, the establishment has started regular monthly audits of stored samples which includes traceability checks of the sample order form, records of sample storage location on the database and sample storage location in the freezer (see advice item 5).

The establishment disposes of human samples by incineration. Records of disposal are made by recording the date for disposal (see advice items 14 & 15).

The DI, Corporate Licence holder contact (CLHc), Health and Safety officer and Person Designated (PD) have regular governance meetings and are responsible for the overall governance of the storage and use of human tissue samples under the HTA licence.

The site visit inspection included a visual inspection of the areas where relevant material is stored under the licence, a review of documentation and meetings with establishment staff. An audit was conducted of four samples of extracted and expanded PBMCs. These audits revealed no anomalies in the storage locations or sample identifiers recorded on the electronic databases.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	The establishment has no overarching governance framework. There are insufficient documented policies and SOPs to reflect the procedures and practices associated with the activities carried out under the licence including the transportation of human tissue samples from the supplier to the establishment. The current standard operating procedures (SOPs) relate only to lab protocols for sample processing and disposal. *(See advice item 3)*	**Major**
GQ2 There is a documented system of quality management and audit.	The establishment does not have a documented system of quality management and there is no document control system. As noted in the GQ1 findings, the establishment does not have most of the SOPs relevant to the HTA licence. At the time of inspection, there were two SOPs relevant to HTA licensable activities. These documents had inconsistent document control information. For example: • COSHH risk assessment form had appropriate document control such as version number, effective date, next review date; however, the document was not signed by the assessor, safety officer or the line manager; and, • The SOP for disposal of CAT II waste lacked version number, effective date, next review date and name of approver. *(See advice item 4)*	**Minor**
GQ7 There are systems to ensure that all adverse events are investigated promptly.	There is no system or formal procedure in place to report or investigate adverse incidents which may relate to the loss of tissue, loss of traceability or sample mix up. *(See advice item 7)*	**Minor**

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	Although the establishment has conducted a risk assessment on the use of human tissue, this focuses on the health and safety risks associated with this activity. The risks associated with the carrying out of licensable activities have not been formally risk assessed. *(See advice item 8)*	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.	The human tissue is stored in an unlocked freezer, with local alarm and security staff patrol the building out-of-hours. The local alarm system for the freezer unit is not subject to routine testing. Additionally, there are no formal out-of-hours arrangements in the event of freezer breakdown and freezer temperatures are not remotely monitored. As such, there is a potential risk to the integrity of stored samples in the event of freezer failure left unattended over an extended period of time. The functionality of the alarm system and the responsibilities of the security staff and any risks associated with these have not been clearly documented. *(See advice items 10 & 11)*	**Minor**

Disposal

Standard	Inspection findings	Level of shortfall
D1 There is a clear and sensitive policy for disposing of human body parts and tissue.	There is no disposal policy in place for disposing of human tissue samples. At the time of inspection, the establishment had two existing disposal SOPs, which described inconsistent disposal procedures for disposal of both solid and liquid human tissue waste. The existing SOPs for disposal do not reference (or detail) either the HT Act or Code of Practice (CoP) on Disposal requirements. *(See advice item 14)*	**Minor**

Advice

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

No.	Standard	Advice
1.	C1	The establishment is in the process of renewing the material transfer agreement with NHSBT. DI is advised to document the checks that will be performed when evaluating a third party supplier of relevant material. For example, the DI may wish to produce a checklist to use when reviewing third party suppliers. This will help to strengthen the establishment's assurance that the consent for the use of samples for research is in accordance with the requirements of the HT Act and the HTA's CoP on Consent.
2.	C1	The establishment has previously considered obtaining blood samples from members of staff. In the event that the establishment decides to start blood collection from members of staff, the DI is advised that he will need to develop a consent policy, consent forms and carry out risk assessments in line with the HT Act and HTA's Codes of Practice.
3.	GQ1	The DI is advised to develop policies and SOPs pertaining to HTA licensed activities to ensure that these reflect the procedures and practices carried out under the licence. These SOPs should cover the following areas: • sample collection; • relevant arrangements for the transport/transfer of sample; • sample receipt; • storage of samples, which includes how the samples will be labelled, recorded on the database and relevant storage temperatures; • cleaning of storage areas and decontamination. • secure management of records and data retention; • maintenance of storage facilities; • incident management system which describes reporting and recording any non-conformances and their follow up by corrective and preventative actions (CAPAs); and, • carrying out audits.
4.	GQ2	The DI is advised to consider the inclusion of the following features to each document to improve document management: • document control information, such as a revision history and version number; • review date (at least every two years); • issue date; • pagination; and, • the names of both the author and the reviewer who has authorised the content of the document (the reviewer should have knowledge of the relevant procedure/process but need not be more senior than the author). The DI is also advised to ensure that all staff working under the licence have read the SOPs and that this is recorded.

5.	GQ2	The establishment has recently started to carry out audits covering the traceability of sample receipt and storage. The DI is advised to expand the scope of the audits to include: • Audits of records of sample transport, use and disposal of relevant material; • storage temperature; and, • Back-up of the sample database. The DI is advised to document these audits to ensure that any non-conformances can be identified and discussed in the governance meetings for the HTA licence. All audit findings and related corrective and preventative actions should be recorded to allow the establishment to demonstrate compliance with HTA standards and follow-up outstanding actions.
6.	GQ3	The establishment has a health and safety staff training procedure in place. The DI is advised to develop a training package for staff who are involved in undertaking licensed activities. The DI is advised to consider introducing refresher training for staff periodically thereafter. The DI may wish to refer to the e-learning package developed by the Medical Research Council in conjunction with the HTA covering the requirements of the HT Act for the research sector: www.rsclearn.mrc.ac.uk/ .
7.	GQ7	The DI is advised to implement a local reporting system for incidents and non-conformances, and to detail any actions taken. Examples of such incidents and non-conformances could include: • loss of sample; • loss of sample integrity; • loss of sample traceability; • Freezer malfunction; • Missing or incorrect documentation; • database not updated or backed up; • security breach; and, • inappropriate disposal
8.	GQ8	The DI should document risk assessments for the risks associated with the storage of human tissues and non-compliance with the HT Act. These risks may include, for example: • storage and use of relevant material without appropriate consent; • storing or using human tissue after consent withdrawal; • loss of human tissue; • sample mix-up or loss of traceability of relevant material; • failure of storage facilities or other damage affecting human tissue quality for useful research; • transport of specimens to and from establishment; • security arrangements; and, • accidental or inappropriate disposal of relevant material.

		The DI is advised to ensure that risk assessments are reviewed regularly and that all staff undertaking licensable activities are aware of these risk assessments.
9.	PFE2	While environmental controls are in place, and the establishment is subject to a regular cycle of health and safety audits, the DI is advised to consider documenting a cleaning schedule for the storage areas.
10.	PFE3	The DI is advised to ensure that freezer temperatures are checked and recorded on a regular basis The DI is also advised to ensure that there is routine testing of storage freezer temperature alarm. The establishment may wish to consider storing these temperature records near to the storage units so that staff are aware of when these checks have been performed.
11.	PFE3	While an informal arrangement is in place for the security guards to patrol the building and check the freezer alarm during out-of-hours, there is no formalised agreement in place with the security company. The DI is advised to document the responsibilities of the security staff during out of hours.
12.	PFE4	Currently, the human tissue samples are transported in a private vehicle by a member of staff. While addressing the shortfalls set out against GQ1 and GQ8, the DI should risk assess this process and document the procedure for the transportation of human tissue samples.
13.	PFE5	The establishment used to have a formal agreement with a maintenance company for the regular maintenance of the freezer, which expired in August 2014. The DI is advised to put a formal agreement in place to ensure timely maintence and calibration of the equipment, in order to reduce the risk any loss of human tissue samples due to equipment failure.
14.	D1	The DI should develop a disposal policy and relevant procedures, which comply with Health and Safety recommendations and refer to the HTA CoP on Disposal. The DI is also advised to review the current disposal SOP to ensure that the disposal guidelines cover the disposal of liquid and solid waste and that only the current version of disposal SOP is in use. To facilitate the document control, the DI is advised to include a version number on the SOP.
15.	D2	The establishment has a system to record the disposal of human tissue in the sample database. The DI is advised to ensure the method and reason of disposal is recorded along with the date of disposal.

Concluding comments

This report outlines the first HTA site visit inspection of F-Star Biotechnology. There were a number of areas of good practice observed during the inspection. The Designated Individual is well supported by the Person Designated and together, they have a good oversight of licensable activities undertaken at the establishment. There is a good sample traceability and although the expanded PBMCs no longer contain cells that originated in the human body, the establishment maintains traceability of these cultured cells to the point of disposal.

There are a number of areas of practice that require improvement, including one major and five minor shortfalls in relation to the development of the overarching governance documents, document control systems, audit and risk assessments of both the premises and the practices; and disposal of human tissue samples. The HTA has given advice to the DI with

respect to consent, governance and quality arrangements and the premises, facilities and equipment and disposal.

The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan 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: 13 July 2015

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

Final report issued: 31 July 2015

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 December 2015

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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management

committees, agendas and minutes

- Complaints system

GQ2 There is a documented system of quality management and audit

- A document control system, covering all documented policies and standard operating procedures (SOPs).
- Schedule of audits
- Change control mechanisms for the implementation of new operational procedures

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills

- Qualifications of staff and training are recorded, records showing attendance at training
- Orientation and induction programmes
- Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training
- Training and reference manuals
- Staff appraisal / review records and personal development plans are in place

GQ4 There is a systematic and planned approach to the management of records

- Documented procedures for the creation, amendment, retention and destruction of records
- Regular audit of record content to check for completeness, legibility and accuracy
- Back-up / recovery facility in the event of loss of records
- Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ5 There are documented procedures for distribution of body parts, tissues or cells

- A process is in place to review the release of relevant material to other organisations
- An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail

- There is an identification system which assigns a unique code to each donation and to each of the products associated with it
- An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom

GQ7 There are systems to ensure that all adverse events are investigated promptly

- Corrective and preventive actions are taken where necessary and improvements in practice are made
- System to receive and distribute national and local information (e.g. HTA communications)

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately

- Documented risk assessments for all practices and processes
- Risk assessments are reviewed when appropriate
- Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards

PFE1 The premises are fit for purpose

- A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose
- Policies in place to review and maintain the safety of staff, authorised visitors and students
- The premises have sufficient space for procedures to be carried out safely and efficiently
- Policies are in place to ensure that the premises are secure and confidentiality is maintained

PFE 2 Environmental controls are in place to avoid potential contamination

- Documented cleaning and decontamination procedures
- Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination
- Appropriate health and safety controls are in place

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.

- Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination
- Contingency plans are in place in case of failure in storage area
- Critical storage conditions are monitored and recorded
- System to deal with emergencies on 24 hour basis
- Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination

- Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation
- A system is in place to ensure that traceability of relevant material is maintained during transport
- Records of transportation and delivery
- Records are kept of any agreements with recipients of relevant material
- Records are kept of any agreements with courier or transport companies

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored

- Records of calibration, validation and maintenance, including any agreements with maintenance companies
- Users have access to instructions for equipment and receive training in use and maintenance where appropriate
- Staff aware of how to report an equipment problem
- Contingency plan for equipment failure

Disposal Standards

D1 There is a clear and sensitive policy for disposing of human organs and tissue

- Documented disposal policy
- Policy is made available to the public
- Compliance with health and safety recommendations

D2 The reason for disposal and the methods used are carefully documented

- Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal
- Where applicable, disposal arrangements reflect specified wishes

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.