Site visit inspection report on compliance with HTA minimum standards

Sygnature Discovery Limited

HTA licensing number 12614

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**

4 November 2014

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.

Sygnature Discovery Limited (the establishment) was found to have met all HTA standards.

Particular examples of strengths and 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 licences 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

Sygnature Discovery Limited (the establishment) is a commercial clinical research organisation providing contract research focusing on novel drug discovery using *in vitro* cell models and biochemical based assays. All research is in response to client requests with no in-house directed research conducted.

The establishment currently stores serum and human derived cell lines. On the day of inspection, none of the material held by the establishment was classifiable as relevant material and therefore fell outside the remit of the Human Tissue Act 2004 (HT Act). Despite this, the establishment have decided to treat all material as HT Act relevant material.

The establishment is planning to implement a Blood Donor Panel in the future and provided the relevant draft documentation. Blood donors will be found from volunteer staff at the establishment. A phlebotomy service company will be contracted to draw blood from volunteers. It is planned that whole blood samples will be used to either isolate serum after exposure to drug compounds or cellular components of the blood will be isolated for *in vitro* assay use. Recruitment of staff participants will be via an internal email. If the number of required participants is not obtained, a further email requesting participants will be sent. Participants will be monitored for frequency of blood donations to ensure they do not exceed safe limits for donations.

The establishment purchases human derived live cell cultures from commercial suppliers. Prior to ordering of these cell lines, a risk assessment form is completed by the member of staff requesting the cells, this is reviewed by an internal panel. If approved, the cells are ordered using the in house system and a unique order code for human derived cells is applied to the order. This code alerts the technician responsible for collecting orders that human derived cells are expected. On the day of delivery, the shipment of human-derived cells is collected in person from the courier and signed for by a designated technician. The technician then delivers the cells to the person who ordered them.

Whole bloods received from clients are processed as requested on the day of receipt. Samples are then stored for no longer than overnight before being centrifuged to produce serum. It is the expectation of the establishment that the centrifugation step is sufficient to remove all cells from the supernatant. The supernatant layer (serum) is removed and aliquoted into 96 well plates or small cryovials and stored in a designated -80^{o}C freezer. The cell containing pellet fraction is decontaminated and disposed of. The processing procedure is recorded in the electronic lab book of the individual responsible for the processing as well as on the electronic inventory log.

There is one -80^{o}C freezer and one liquid nitrogen dewar where the establishment holds human serum and human derived cell lines, respectively. All storage facilities are located in secure areas of the premises with restricted access. There is one -80^{o}C freezer and two liquid nitrogen dewars as contingency back-up storage. The -80^{o}C freezers have a local alarm system and are periodically checked by staff. The level of liquid nitrogen in the dewar is checked and manually recorded three times per week, Monday to Friday. If the level falls below a set limit, the liquid nitrogen dewar is topped up. Site security staff are present from 6am until 10pm and perform routine checks throughout the building. If a freezer is found to be alarming outside normal working hours, a designated staff member of the establishment is contacted by security. Failure of a freezer outside the hours of security staff presence relies on the manufacturer's assurance that the freezer should maintain temperature under normal conditions and if left closed for ten to twelve hours. Electronic inventories are kept for each storage facility, recording the location and numbers of samples.

The establishment has been licensed by the HTA since February 2014. This report describes the first, routine, site visit inspection of this establishment. The timetable for the site visit inspection was developed in consideration of the establishment's licence application and pre-inspection discussions with the DI. The site visit inspection included a visual inspection of the cell receipt and storage areas, a review of documentation and meetings with establishment staff. The inspection team conducted interviews with the DI, Chief Operating Officer and Principal Scientist for Biosciences. An audit of traceability records, including electronic databases and storage locations was conducted for two unique samples stored in the -80^{o}C freezer. All samples were chosen at random by the inspection team. No anomalies were identified and all electronic records and storage locations were consistent. Additionally, an electronic audit was undertaken using cell identifiers from the main inventory log which were then compared against details held within a separate, liquid nitrogen dewar map/inventory.

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

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	C1	The establishment does not currently seek consent from the donors of samples. In the future, the establishment plans to implement a Blood Donor Panel. The proposed consent form does not include details regarding withdrawal of consent for the sample taken. The DI is advised to review the proposed consent form and include a statement to give the donor information regarding withdrawal of consent and what would be possible.
2.	C1	Informed consent is not currently sought by the establishment. However, if the establishment were to implement the planned Blood Donor Panel using staff volunteers, a formal training program for those seeking consent would need to be developed. This training would need to be in accordance with the requirements of the HT Act 2004 and the HTA's Code of Practice. The DI is advised to develop a consent training program for all staff who will be seeking consent.
3.	C2	No Participant Information Sheet has been developed with regards to donating blood for use in the Blood Donor Panel. The DI is advised that a Participant Information Sheet should be provided to each donor to help fully inform them about participation in the donor panel and what is involved.
4.	GQ1	Currently, any issues surrounding human tissue are discussed at the bi-weekly Biosciences group meeting which the DI attends. These meetings are not minuted. The DI is advised to either have an independent meeting to discuss HTA matters or minute the current Bioscience meetings.
5.	GQ2	At present the DI carries out routine audits of sample locations compared to electronic inventories. These audits are not scheduled or recorded. The DI is advised that a schedule of audits should be created and, when conducted, the audit findings are recorded.
6.	GQ2	The proposed consent form and policy entitled 'A process for requesting human volunteer blood' is not version controlled. The DI is advised that all documents need to be version controlled to help ensure that only current versions are in use.
7.	GQ2	Currently audits are undertaken on a non-scheduled basis and are not recorded; no corrective and preventative actions (CAPA) plans are created as a result. The DI is advised that audits should be scheduled, recorded and CAPA plans devised from the findings.

8.	GQ3	The establishment currently undertakes staff training with regards to the use of human tissue with an emphasis on biological safety aspects. The DI is advised this training needs to be broadened to include the importance of traceability, recording/reporting adverse events and recording of the disposal of human tissue.
9.	GQ6	Currently, the number of 96-well plates or vials prepared from a receipted sample is not recorded in the electronic lab books of establishment staff. The original sample volume and treatment of the material is not recorded in real time but is recorded in individual electronic lab books. These must be written up no longer than two weeks post processing. The DI is advised all treatment and processing of relevant material should be recorded in real time to ensure no lapse in traceability occurs.
10.	GQ8	The establishment has risk assessments, which cover issues of health and safety and COSHH; however they do not include risks relevant to the integrity, loss or contamination of human tissue. The DI is therefore advised to review all current risk assessments to ensure these types of risks are covered.
11.	PFE3	The -80^{o}C storage facility possesses a local alarm which is triggered when the temperature deviates outside set ranges. The liquid nitrogen dewar has no alarm but levels are checked and manually recorded three times per week, Monday to Friday. The DI is advised to develop and implement a system whereby the establishment staff would be alerted to a temperature deviation outside set temperature ranges outside of normal working hours. The DI is advised to manually challenge this system regularly to ensure that it is working to required specifications. These challenges and outcomes should be recorded.
12.	PFE5	Currently there are no signs on storage areas containing human material to alert general users of its presence. The DI is advised to add signs to storage areas to indicate the presence of human material to make staff aware of its presence and to ensure storage area is easily identified.

Concluding comments

This report outlines the first HTA site visit inspection of Sygnature Discovery Limited. The establishment has a strong commitment to the continual improvement of practices and compliance with the Human Tissue Act (HT Act). The DI and staff demonstrate a conscientious approach to the handling and traceability of relevant material. The Designated Individual is well supported by the Principal Scientist of Biosciences; together they have good oversight of activities undertaken at the establishment. Although the cell cultures and serum stored and used by the establishment are not considered relevant material under the HT Act, the establishment maintains traceability of these cells in both liquid nitrogen storage and the -80^{o}C freezer to the point of disposal. All equipment is well maintained and under service contracts.

The HTA has given advice to the Designated Individual with respect to consent, governance and quality systems and storage facilities.

The HTA has assessed the establishment as suitable to be licensed for the activities specified

Report sent to DI for factual accuracy: 19 November 2014

Report returned from DI: 02 December 2014

Final report issued: 03 December 2014

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.