Site visit inspection report on compliance with HTA minimum standards

Synairgen Research Limited

HTA licensing number 12532

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**

16 October 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.

Synairgen Research 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

Synairgen Research Limited (the establishment) is a commercial company providing clinical and non-clinical operations focused on the development of novel therapies for respiratory disease. They have developed a biobank of clinical samples obtained from volunteers recruited for clinical trials. They have developed *in vitro* cell models to aid the discovery of novel drug targets, to identify the molecular mechanisms in asthma and chronic obstructive pulmonary disease (COPD), and for support of clinical trial activities.

The establishment stores whole blood, plasma sputum, biopsies, nasal and bronchoalveolar lavages, throat swabs and brushings. The establishment treats human derived cell lines and plasma in the same manner as relevant material under the Human Tissue Act 2004. Samples are obtained on site within the Wellcome Trust facility of Southampton General Hospital by trained clinical staff.

Recruitment of participants is primarily via poster and radio advertisement. Samples are used for analysis of mediators, to produce cell cultures for *in vitro* cell assays or are fixed and sectioned for immunohistology analysis. Participants who contact the establishment to enrol in the clinical study are initially assessed for eligibility against predetermined and Research Ethics Committee (REC) approved criteria. Those who are deemed to be eligible to participate are sent participant information sheets and consent forms an appropriate amount

of time prior to sample donation. Consent is taken by a clinician and witnessed by at least one of the Synairgen Research Limited Clinical Team staff members.

Samples taken are labelled with the study reference number, an unique identification code and the date. Samples are then transported by a member of the non-clinical team to the laboratory for processing. Samples are recorded on both paper records and an electronic database. Samples for cell culture are expanded and then frozen down and stored in liquid nitrogen dewars. Samples that have been fixed for immunohistological examination are stored at either 4^{o}C or -20^{o}C. Other samples such as blood, plasma and sputum are stored at -80^{o}C.

There are four -80^{o}C freezers, two liquid nitrogen dewars, one 4^{o}C fridge and one -20^{o}C freezer all holding relevant human material. All storage facilities are located in secure areas of the premises, with restricted access, and are locked. One of the -80^{o}C freezers is a dedicated Research Tissue Bank for which the company has REC approval. All storage facilities are continuously temperature monitored and have alarm systems in place for temperature deviations outside set acceptable ranges. The -80^{o}C freezers and liquid nitrogen dewars have wireless system alerts for deviations outside set ranges, which contacts four members of the non-clinical team. Two members of staff always attend the site if a freezer alarm is activated. Manual recordings of freezer temperatures are performed twice weekly Monday to Friday. Each storage facility is identified with a unique number and has its own inventory electronic record log recording location of samples.

The establishment has been licensed by the HTA since November 2008. 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, compliance update information and pre-inspection discussions with the DI and PDs. The site visit inspection included a visual inspection of the cell processing and storage areas, a review of documentation and meetings with establishment staff. The inspection team conducted interviews with the DI, Head of Laboratory, Senior Research Scientist and Head of Clinical Operations and Senior Research Nurse. An audit of traceability records, including paper-based, electronic databases and storage locations was conducted for five unique samples stored in the various storage facilities. All samples were chosen at random by the inspection team. Anomalies were identified in electronic based records for the freezer storage location and number of aliquots of the one of the -80^{o}C freezer samples. The storage location was absent for the 4^{o}C and -20^{o}C stored samples, however due to only a single possible storage location for these samples traceability was maintained. All other electronic records and storage locations were consistent and traceability of samples was maintained.

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 demonstrated good practice with regards to their consent seeking process. Members of the clinical team witness consent being taken by the clinician. However the current SOP could be improved to reflect this practice by detailing the process more accurately.
2.	GQ1	The establishment treat all cultured samples as relevant material. The current 'Respiratory Tissue Bank Laboratory Manual,' states the temporary location of cultures is not recorded. This, however, seems to be in discordance with staff practice. The DI is therefore advised to review the manual to reflect staff practice and thus ensure continued traceability of samples.
3.	GQ1	Some documentation required correcting to reflect the Human Tissue Act 2004 legislation. For example, one document inaccurately stated that samples obtained prior to 1st September 2006 are not considered relevant material. This document also states material released from the Research Tissue Bank (RTB) can only be sent to establishments licensed by the HTA. This is not a requirement of the HTA; the DI is advised to seek confirmation of any restrictions imposed by the Research Ethics Committee who issued the RTB approval.
4.	GQ3	The DI is advised to review the format of training records for non-clinical team members to include 'Acknowledgement of training' forms in training records as seen in the Head of Clinical Operations training record.
5.	GQ6	The electronic database system does not currently record location of fixed samples stored at 4°C and -20°C, thus relying solely on knowledge of staff. The DI is advised to utilise the existing features of the database to ensure that the storage locations of all relevant material is being recorded.
6.	GQ6	Discrepancies were observed between freezer map location records, number of aliquots and physical locations of audited samples. The DI is advised to review the current procedure for sampling location recording and to undertake regular traceability audits to identify any discrepancies in records.
7.	GQ8	The establishment includes the risk assessment at the start of their SOPs. These 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.

8.	PFE3	The establishment has a robust alarm system which alerts 4 members of staff if the freezer falls outside of established limits. The DI is advised to manually challenge the alarm system on a regular basis to provide assurance that the system and procedure functions as expected. The DI is advised to record the findings of such a challenge.
9.	PFE3	The DI is advised to review the current -80^{o}C freezer storage system of a single tray to store a large number of cryovials. This would help to identify the risks posed by a heavy tray, either to the samples or to the staff; for example, should the tray be dropped.

Concluding comments

This report outlines the first HTA site visit inspection of Synairgen Research Limited. There were a number of areas of good practice observed during the inspection. The establishment has a strong commitment to the continual improvement of practices and compliance with the Human Tissue Act 2004 (HT Act). This was particularly evident in the oversight and recording of training of all staff who are involved in licensable activities. Staff demonstrate a conscientious approach to the handling and traceability of relevant material. This was shown on the day of inspection by the team actioning the addition of the storage location in electronic records for the samples stored at 4^{o}C and -20^{o}C prior to departure of the inspection team. The Designated Individual is well supported by three Persons Designated; together they have good oversight of licensable activities undertaken at the establishment. Although cell cultures produced from biopsies contain only cells which have divided outside the human body, and are therefore no longer considered relevant material under the HT Act, the establishment maintains traceability of these cells in both liquid nitrogen storage and fixed samples on slides to the point of disposal. The consent-seeking process is conducted by clinical staff based at the hospital and witnessed by two members of the clinical team. There is a good and high quality set of documents. Quality assurance checklists are included in the back of SOPs for reviewers to complete prior to signing. Risk assessments are included in the front of SOPs to ensure staff have read both documents relating to procedure. Equipment is the property of the University of Southampton and is therefore maintained by them. However, to ensure equipment is not missed from maintenance routines, the establishment keep their own equipment maintenance tracker.

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: 5 November 2014

Report returned from DI: 7 November 2014

Final report issued: 11 November 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.