Licence application visit on compliance with HTA minimum standards

Autolus Limited

HTA licensing number 12642

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**

13 October 2015

Background

A licence application visit was carried out of Autolus Limited ('the establishment'). A visual inspection of the premises, included the laboratory where human tissue will be handled and the storage area where human tissue will be stored. There are two liquid Nitrogen tanks and three -80C freezers. The critical storage conditions are continuously monitored and freezers and liquid nitrogen tanks alarmed. At the time of the visit, one -80C was in operation. The plan is to use one -80C freezer for contigency purposes. Discussions took place with the prospective DI and his team in regards to quality management systems, consent, audit and risk assessments.

The establishment will be involved in purchasing peripheral blood from NHS BT that will be stored and used for research. The establishment is already involved in an ethically approved project with NHS BT involving leucopheresis under ethics (REC reference). There are also plans to include staff as participants in research involving human tissue.

Advice

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

No.	Standard	Advice
1.	C1/PFE4	The establishment will purchase peripheral blood from third party providers which will be transported using a courier organised by the third party. The establishment will receive a template consent form from the third party provider to indicate that consent was given for research purposes. The DI is advised to consider putting in place an agreement or amending current agreements in order to provide an assurance that only human tissue that has been consented for research purposes will be provided to the establishment. **Action:** DI to provide a copy of this. (Minor shortfall, C1/PFE4)
2.	C2	Staff working at the establishment may be involved in human tissue research. Researchers wishing to use human tissue from staff (i.e. blood) will be required to go through a formal application process which will be reviewed by the Health and Safety Committee. Once granted with an approval to collect blood, researchers will advertise their research on the premises and are not permitted to approach staff personally. The research undertaken could give rise to clinically significant results or incidental findings. The DI is advised to discuss this issue with clinical professionals to seek advice on any ethical considerations of sharing results. The DI should also consult the framework that the MRC and Wellcome Trust have put in place for ' health related findings'. This aspect should be built into the information sheet and consent form so that the participant is fully informed about incidental findings that could arise and how these may be handled. **Action:** To review on site visit inspection
3.	C3	Phlebotomists involved in seeking consent should be trained for this purpose. The DI should devise a consent training programme for all staff involved in seeking consent as well as for new members of staff. Refresher consent training should also be considered. This training could be integrated into an induction programme for all new staff as well as part of continuous professional development. **Action:** DI to provide assurance that this is in place prior to commencing staff based research. (Minor shortfall, C3)
4.	GQ1/GQ2	The DI has drafted the following SOPs: 1) Waste Dispoal and Decontamination, version 01, POL-0013

		2) In lab controlled temperature storage, version 0.1, AES-0001 3) Approval and collection of donor samples for laboratory research, version 0.1, POL-0008 4) Donor consent, version 0.1, FRM-0001 5) Application for donation samples form, version 0.1, FRM-0002 6) Accidents, near misses and reporting, version 0.1, POL-0007 7) Security, version 0.1, POL-0011 8) Staff training, version 0.1, POL-0010 9) Emergency Evacuation, 0.1, POL-0005 **POL-0008** This is a really important document that outlines the activities and procedures that need to be followed when using fresh blood samples. The procedures have particular focus on how to prepare to carry out staff based research. The DI must update the SOP to include comprehensive information about sample receipt from third parties. This could include: i) sample ordering ii) sample reception from the courier, iii) logging the sample on the traceability database, iv) assigning a unique reference number, v) paperwork supporting the sample (i.e. consent templates) vi) placing the sample into storage. The DI should also remove any reference for SAEs to be reported to the HTA as this is not a requirement under the HT Act 2004. This is a requirement under the Human Tissue (Q&S for Human Application) Regulations 2007. **FRM-0001 (Consent)** The staff member will remain anonymised to the researcher. The phlebotomist that will be involved in collecting blood from the participant will be responsible for placing the donor sample number to (page 3) of the consent form as well as page 4. Page 4 will be provided to the researcher. The DI is advised to update page 3 of the form, so that it is clear who consented the participant. To maintain anonymity the DI should consider updating POL-0008 to reflect that the phlebotomist should ensure that the donor ID labels are affixed to the forms once the donor leaves the room. This is to ensure that the participant is unable to link back to their data.

		POL-0007 The DI should consider updating the existing procedure to include dealing with incidents that may impact tissue traceability and integrity. **POL-0010** The Staff training policy is generic. The DI is advised to consider including training for staff involved in human tissue licensable activities. The DI should include the following points: 1) Type of induction that will be received by staff involved in licensable activities. 2) Documented procedures that will need to be read and understood by staff involved in licensable activities. 3) Observation or competency assessment of staff using human tissue in the laboratory setting. 4) Mock experiments using human tissue to ensure staff are following procedures. 5) A formal sign off procedure to demonstrate staff competency. The following SOPs are outstanding: 1) Cleaning and decontamination The DI is advised to draft an SOP which covers cleaning and decontamination. This could be set our in an overarching SOP about Equipment Maintenance. This SOP should also cover alarm set points, testing of alarms, temperature monitoring/trending, actions to be taken if the alarm is sounding during and out of hours and how long the freezers are able to maintain temperature. 2) Audits and CAPAs Once the establishment is operational, the DI should develop an audit schedule. An SOP should be drafted to outline how audits are performed, who performs them, how often, how are non-conformities dealt with and how actions are followed up and closed. 3) Seeking consent Staff involved in research will be consented by phlebotomists taking blood for research purposes. An SOP should be drafted to outline the procedure that phlebotomists must follow in order to seek consent. It should include reference to the HTA Code of Practice 1, Consent, principals, as well as the procedure to be followed: i) approach to participants, ii) time given for participants to decide to take part, iii) forms

		that will need to be completed, iv) points for the consenter to cover with the participant, v) consent withdrawal, vi) consent training **Action:** DI to provide a copy of the updated and new SOPs. Staff research should not start until procedures are in place. (Minor shortfall, GQ1)
5.	GQ8	The DI has carried out a health and safety risk assessment of handling biological material. The DI should extend the scope of risk assessment to cover licensable activities, such as risks to the tissue. For example, loss of tissue traceability, sample mix up, sample loss, critical storage failure, human tissue used without consent etc. Action: DI to provide a copy of this. (Minor shortfall, GQ8)
6.	PFE3	The DI is advised to include the following signage on the -80C freezers and liquid Nitrogen tanks: i) Human tissue or Relevant material storage. ii) The alarm temperature set points (i.e. lower and upper limits). iii) Freezer map to indicate the locations of samples. Action: To review on next site visit inspection.
7.	PFE5	The -80C freezers and the liquid Nitrogen tanks are new and will be under warranty for a few years. In future, the DI is advised to set up a maintenance contract to plan for servicing of the equipment. Action: To review on next site visit inspection.

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: 4 January 2016

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.