Site visit inspection report on compliance with HTA minimum standards

Retroscreen Virology Ltd

HTA licensing number 12594

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**

21 August 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.

Retroscreen Virology Ltd (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

Retroscreen Virology Ltd (RVL) is a contract research organisation and commercial investigator site located in Queen Mary BioEnterprises' Innovation Centre in London. The establishment undertakes clinical trials and translational research into antiviral drugs and vaccines. RVL is the corporate licence holder, the DI is a senior virologist and the corporate licence holder contact is the CEO of RVL. The clinical trials are sponsored by industry, government and academic institutions and have involved over 1,800 volunteers. RVL clinical trials follow a 'viral challenge model' where volunteers are kept in specifically designed quarantine suites and infected with viruses. The course of the infection and the effects of any therapy given to the volunteers are monitored over several weeks. During this period, samples such as blood and nasal fluids and phlegm are taken from the volunteers and analysed.

Volunteers are recruited at several sites including London, Manchester and Ely. Medical staff undertake face to face interviews with potential volunteers, provide them with information on the studies and seek consent for their participation in the studies. They also seek consent for additional tissue samples from the participants. These samples may be taken during the trial and can be used for research studies which may be outside the scope of the clinical trial. Research on these samples may take place after the clinical trial has ended.

All new staff, receive induction training which covers the Human Tissue Act 2004 (HTAct) and its requirements and the role of the DI. They also receive annual Good Clinical Practice refresher training. Staff undertake on-line MRC training and the certificates are included in their training records. The Learning and Development team, which is part of the HR Department, has responsibility for training and the Regulatory and Quality Governance Department are responsible for undertaking audits.

Medical staff who provide information and seek consent from potential volunteers are provided with training in seeking consent and undergo competency assessements (see advice item 2 below). The consent form for each trial informs potential recruits that separate consent will be sought for samples which will be used for purposes outside the scope of the clinical trial. This consent form is reviewed by a NHS Research Ethics Committee (REC) as part of the research ethics approval process. Volunteers complete the REC approved consent form if they agree to participate in the clinical trial. Volunteers complete an additional consent

form if they agree to donate additional samples for research outside the scope of the trial (see advice item 1 below).

Once a clinical trial is completed, depending on the contract between RVL and the trial sponsor, the tissues are either sent to the trial sponsor, disposed of, or stored at the HTA-licensed premises in London. RVL currently stores around 18,000 samples and does not receive or store tissues from other establishments. Samples are stored in dedicated -80^{o}C freezers which are located in a room with secure access. The temperatures of the freezers are continuously monitored and staff respond in the event of freezer failure. The alarm is triggered when the temperature goes above -60^{o}C. A back-up freezer is available in another part of the building in the event that samples have to be transferred to another freezer. RVL also has an agreement with another HTA-licensed establishment to transfer samples for back-up storage if required.

Samples taken during clinical trials are given unique numbers and are tracked using a computer system. Once the trial is over, if consent is in place, the labelled samples are grouped together and placed in boxes which are stored in the -80^{0}C freezers. The contents of the freezers are noted on paper records ('HTA freezer inventory'). The records include the freezer identification, study number, sample description, cohort, box number, aliquot/intake/group, lab freezer temperature, shelf, rack, drawer box colour, current stock (number of samples in box) and name of the study lead. The HTA freezer inventory does not list individual samples in each box, but lists the total number of samples in each box. Staff record the removal of samples from the storage boxes in the paper records relating to each box (see advice item 3 below). The HTA understands that RVL has not begun to use any of these stored samples for research.

A routine inspection of RVL was undertaken on 21 August 2014. This was the first inspection of the establishment since it was licensed by the HTA in June 2012. The inspection included interviews with the Senior Virologist who is the DI, a study physician, the Director of Regulatory and Quality Governance and the Associate Director of Translational Research.

A document review was carried out. Documents reviewed included: consent forms, information provided to volunteers, SOPs (consent, storage disposal, complaints), policies, training records, audit schedule and facilities audit report, temperature monitoring records, risk assessments, maintenance and service/calibration agreements for the freezers, list of approved couriers who have been audited by RVL and the sample destruction form for use when consent for storage and use is withdrawn.

An audit trail was undertaken. Two blood samples and a nasal swab taken from volunteers in a clinical trial were traced from the storage location in the freezer to paper records (the HTA freezer inventory). Consent documentation relating to participation in the clinical trial and additional consent forms relating to storage and use of the samples after the study period ended were also reviewed. No discrepancies were noted.

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	When consent is sought, volunteers are provided with two consent forms. One form covers participation in the clinical trial and the taking of samples directly relevant to the clinical trial. A second 'Additional samples consent form' covers consent for taking additional samples which may be used in future, as yet undefined, research projects. The DI is advised to review and amend the format of the 'Additional samples consent form' to include boxes within which volunteers can initial to evidence that they have read and agree/do not agree with each key statement on the form, and record whether or not they consent /do not consent to donation of samples. The DI is also advised to ensure that all forms specifically state that the future use of the samples has not been defined, and will be subject to ethical review as appropriate. The forms should also document if consent to storage of samples and DNA analysis has been given.
2.	C3	During induction training, staff are informed of the consent provisions in the HTAct. During the inspection it was noted that slides used during the informed consent training session for consent seekers, which was held on 13 June 2014, did not specifically refer to the consent requirements of the HTAct. The DI is advised to ensure that training material for staff who seek consent, includes references to the HTA and HTAct.
3.	GQ6	RVL currently uses paper records (the HTA freezer inventory) which cover a group of samples contained in each box in the -80^{0}C freezers. The HTA understands that RVL has taken steps to move towards an electronic sample recording system which will cover these samples. In the meantime, the DI is advised to consider developing a system to regularly back up the HTA freezer inventory– *eg* by scanning records at regular intervals. This will reduce the risk of loss of traceability in the event that paper records are misplaced or accidentally destroyed.
4.	PFE2	The -80^{0}C freezers and the probes used to monitor the freezer temperature and freezer alarms are maintained on a regular basis. The DI is advised to consider setting up a system to challenge the probes in order to ensure that the probes are effective and the alarm system responds to any increase in temperature above -60^{0}C.

Concluding comments

The DI, staff in the Regulatory and Quality Governance Department and Translational Research Department appear to work well together as a team. There are good systems in place to ensure that medical staff are trained in seeking consent and receive refresher training. Audits are undertaken which cover record keeping relating to samples in storage; discrepancies are noted and appropriate action taken. Risk assessments identify key risks and note steps which are currently taken or may be taken in the future to mitigate those risks. There are robust contingency arrangements in place which include a freezer in another area of the building and an agreement with another HTA licensed establishment to store samples as well as approved couriers which can be used to transport samples in the event of a freezer breakdown.

The HTA has given advice to the Designated Individual with respect to the 'Additional sample consent forms', specifically referring to the HTA's consent requirements during training of consent seekers, backing up paper records relating to samples in storage, and challenging temperature probes used to monitor the temperature of the -80^{0}C freezers where samples are stored.

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

Report sent to DI for factual accuracy: 9 September 2014

Report returned from DI: 15 Septmeber 2014

Final report issued: 17 September 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.