Site visit inspection report on compliance with HTA licensing standards

hVIVO Services Limited

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**

18 and 19 October 2017

Summary of inspection findings

This is the first inspection of this establishment against the revised HTA licensing standards, which came into force on 3 April 2017. The previous inspection took place in April 2014. The HTA found the Designated Individual (DI), the Licence Holder (LH), the premises and the practices to be suitable in accordance with the requirements of the legislation.

hVIVO Services 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

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

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.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

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. They are grouped under four headings:

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

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, 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 provided.

HTA inspection reports are published on the HTA's website.

Background to the establishment

hVIVO Services Limited (the establishment) is a commercial research organisation which was previously known as Retroscreen Virology Limited. The establishment has been licensed by the HTA since 2012 and changed its name to hVIVO Services Limited in 2015. The hub site is located at Queen Mary BioEnterprises (QMB) in London, with satellite facilities in Ely and Welwyn Garden City. The establishment undertakes clinical trials and translational research into antiviral drugs and vaccines. hVIVO plc is the Corporate Licence Holder, the DI is the Laboratory Director and the Corporate Licence Holder contact is the Chief Executive Officer.

Volunteers are recruited at the London site only. Clinical staff undertake face to face interviews after potential volunteers have been screened using phone call interviews. Clinical staff are responsible for seeking consent from volunteers for inclusion in the study and consent for additional tissue from the study participants.The establishment follows a 'viral challenge model' for it's clinical trials, where study participants are kept in specifically designed quarantine suites on site and infected with viruses. The course of the infection and the effects are monitored over a period of time, between several days and weeks. During this period of quarantine, tissue samples such as nasal wicks, nasal swabs, nasal scrapings and blood are taken. These samples can be used for research studies outside the scope of the clinical trial. Within the terms of the approval from the NHS Research Ethics Committee (REC), research on these samples may take place in the 12 months after the end of study confirmation has been issued by the NHS REC. At the end of the NHS REC approval period, all clinical samples are either disposed of, returned to the study sponsor or transferred to the storage site at Ely, where they are stored for future use under the HTA licence and governance systems. No samples are stored at QMB under the HTA licence.

The establishment stores samples in Ely in two -20°C freezers and 12 -80°C freezers located in three separate 'Zones' at the establishment, all with independent air conditioning systems. Zone one contains the two -20°C freezer units and seven -80°C freezers, while Zones two and three contain two and three -80°C freezer units (respectively). Approximately 75 000 samples, comprising relevant and non-relevant (e.g. purified RNA and serum) material, are stored in 11 of the -80°C freezer units under the HTA governance systems. Another 100 000 samples are stored for projects that have received ethical approval from recognised (e.g. NHS) RECS.

Clinical staff who provide information and obtain consent from potential volunteers are appropriately trained in seeking consent and undergo competency assessments

Description of inspection activities undertaken

This was a routine inspection and the second inspection of the establishment since it was licensed in 2012. The inspection included a visual inspection of the clinical areas and

laboratories at QMB, the storage areas at Ely, discussions and interviews with key staff, and a review of documentation. Interviews were held with the DI, the CLHc, the Clinical Support Specialist, the Principal Research Scientist, and the Laboratory Services and Biobank Manager (PD at Ely). The Welwyn satellite was not visited on this inspection as there is currently no licensable activity being undertaken there.

Samples remaining after completion of a clinical trial will either be disposed of or stored under the HTA licence at the Ely site. The establishment does not differentiate between relevant material and other material, storing everything under the HTA conditions and governance systems. This comprises samples of the original material or aliquots that have been processed and generated from the original sample, e.g. serum, RNA ,and DNA. For the purpose of demonstrating traceability, audits were performed on eight samples; comprising two plasma samples stored at -20°C and six samples in -80°C storage. Samples audited from -80°C storage comprised nasal scrapings, whole blood collected and stored in vacutainer tubes, and purified RNA. While not considered relevant material, the purified RNA was stored under the HTA governance systems by the establishment. The samples were randomly selected from different locations within the storage facilities and labelling and location details were compared with the electronic and paper records. Samples were audited both from record to location, and from samples randomly identified in storage back to their electronic and paper records. Of the eight samples audited, two were from the -20°C freezer and two from a -80°C freezer in Zone one, while two samples were audited from a -80°C freezer in Zone two and two samples from a -80°C freezer in Zone three. There were minor issues with four of the eight samples audited, but all discrepancies could be resolved by further investigation of the source records (see *Advice*, item 5).

Inspection findings

The HTA found the Licence Holder, the Designated Individual and the premises 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 (d)	The participant information sheet, reviewed for content, provided contact details for study staff but did not specifically provide information about how a participant could withdraw consent. The DI is advised to ensure that the ability to withdraw consent is specifically covered in the participant information sheet.
2.	GQ1 (a)	The DI is advised to remove information regarding HTA SAEARs from the 'Human Tissue Act' document as this information is relevant only to establishments licensed in HTA's 'Human application' sector.
3.	GQ6 (a)	When a new study is initiated, risk assessments are performed for individual aspects of the study, and copies are kept in the Study Master File. However, within the maximum of 12 months between the time of study completion and longer term licensed storage, the post-study risks to retained samples are not assessed. The DI is advised to develop post-study risk assessments, covering the risks associated with the storage of samples that are no longer associated with a specific study.
4.	GQ2 (a)	Once a study is completed, remaining samples are either disposed of or transferred to Ely for long term storage under the HTA licence. Currently, these samples are not used but may be used for future studies, in accordance with their associated consent. As a result, freezers are only accessed to store samples, and no sample audits are performed to limit access to the freezers. The DI is advised to implement a system where boxes of samples adjacent to a new box can be audited when it is placed in the freezer. This will limit access to the freezers while allowing for audits of stored samples.
5.	T1 (a)	Samples are tracked through the lifecycle of a study using paper records. These form the source documents used to record their locations at Ely once they are under the HTA licence. There were inconsistencies, likely due to transcription errors, between the location noted on the paper and the physical location in the freezers. While the sample box name could be indentified from the paperwork, reliable identification often required the analysis of a combination of several details on the paper, and was hand written in an inconsistent manner. Documentation that could be used to trace back details to the samples was held in the clinical study folders and staff at Ely had generated an electronic database for day to day sample tracking and recording spaces in the freezer units. The DI is advised to review the sample tracking process and advance plans to implement an electronic system for routine

		sample tracking. As an interim measure, the DI should consider expanding the existing electronic database and formalising its use.
6.	T1 (d)	After telephone screening, volunteers are assigned a Patient ID and brought into the clinic for panel screening to identify baseline characteristics. Volunteers are identified as eligible for a new study based on the panel screening and will then be assigned a randomisation number, specific to the study. On clinical collection, samples may be identified using either the Patient ID or randomisation number. This has resulted in samples being assigned either number and being mixed together in the sample box, even at late stages of the study. The DI is advised to review this process and implement a consistent and reproducible labelling system.

Concluding comments

This report outlines the second routine inspection of the establishment. A number of strengths and areas of good practice were observed during the inspection, including:

- The same local procedures are used at both the hub and satellite for all samples, whether samples are being stored under the HTA licence or under project-specific ethical approvals from recognised RECs.

- The establishment has generated a large suite of appropriate SOPs that are limited to a maximum of five pages. They have used flowcharts to visually explain procedures.

- The establishment appears to have a highly organised team that works well together and regularly communicates, effectively, across the different sites.

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

Report sent to DI for factual accuracy: 15/11/2017

Report returned from DI: 24/11/2017

Final report issued: 27/11/2017

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
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
e) Language translations are available when appropriate.
f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
b) Records demonstrate up-to-date staff training.
c) Competency is assessed and maintained.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.
b) There is a document control system.
c) There are change control mechanisms for the implementation of new operational procedures.
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.
e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities.
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training.
b) There are documented induction training programmes for new staff.
c) Training provisions include those for visiting staff.
d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.
b) Risk assessments are reviewed regularly.
c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.
c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity.
b) Where relevant, storage arrangements ensure the dignity of the deceased.
c) Storage conditions are monitored, recorded and acted on when required.
d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
c) Staff are provided with suitable personal protective equipment.

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.