Site visit inspection report on compliance with HTA licensing standards

Mologic Ltd

HTA licensing number 12647

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**

27 June 2018

Summary of inspection findings

The HTA found the Designated Individual (DI) and the Licence Holder (LH) to be suitable in accordance with the requirements of the legislation.

Although the HTA found that Mologic Ltd (the establishment) had met the majority of the HTA's standards, five major shortfalls and eight minor shortfalls were found. These were due to non-compliance in the following areas: consent procedures and training, governance and quality systems, traceability and premises, facilities and equipment.

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

Mologic Ltd is a biotechnology company primarily involved in innovation and development of in vitro diagnostic products. Some research contract work is also undertaken. The establishment is involved in clinical trials that are both ethically and MHRA approved and receive tissue for storage under the governance of this arrangement. The establishment also recruits staff as healthy volunteers who may donate urine, blood and tissue swabs for research and performance assessment purposes. Human tissue may also be purchased from third party tissue providers or acquired from research tissue banks.

The establishment is licensed by the HTA under the HT Act for the storage of relevant material which has come from a human body for use for a scheduled purpose. The establishment stores human samples for use for the scheduled purpose of 'research in connection with disorders, or functioning, of the human body' and for performance assessment purposes. All samples stored at the establishment at the time of the inspection were obtained from living donors.

The establishment has been licensed by the HTA since March 2016. This report describes the first routine inspection of the establishment.

At the time of the inspection, the establishment was storing frozen human samples in six frozen storage units at -80°C; two were located within the main building and four were located in a temperature-controlled secure area adjacent to the main building. Human tissue is also stored in a frozen storage unit at -20°C which is located in a secure laboratory area. Temperatures are recorded manually at the start of the week. There is an automated alarm in the event of a deviation from the set acceptable temperature ranges for all -80°C frozen storage units. The temperature alarm is sounded locally during normal working hours and there is a call-out notification procedure in the event that the alarm is triggered outside of normal working hours. There is no alarm system and call-out procedure for the -20°C frozen storage unit (see shortfall against standard PFE2c). The establishment has contingency arrangements for temperature-controlled storage at -80°C.

The DI maintains oversight of samples stored under the licence. All human samples stored as part of a clinical trial or under ethical approval are anonymised and the unique sample study identifier is used by the establishment to record receipt, use and disposal. The establishment uses a paper storage record to provide a log of all samples. The storage location of samples is not recorded in the sample log but the sample study is mapped to a paper record on the door of the -80°C storage units which are not controlled documents. The precise location of the samples are not recorded but can be traced to the tray position in the storage unit by the paper record on the door. The sample log is scanned approximately twice per year as a back-up record (see shortfall against standard GQ4b).

Healthy volunteer donors are recruited from the establishment by a general email to all staff inviting them to donate blood, urine, saliva and tissue swabs, depending on the study. From expressions of interest, staff are invited to attend a meeting with the consent seeker to outline the research, discuss any risks involved and donors have the opportunity to ask questions (see shortfall against standard C2c). Written consent for donation of blood, urine, saliva or swabs is taken and the volunteer is able to withdraw consent at any time up to the point of use (see shortfall against C1b). The donor will reconsent if continuing to donate blood. Donors are not reconsented for longitudinal studies involving urine or swabs. Urine is often processed and used on the same day as donation. Completed consent forms are stored in a secure location and allocated a unique donor number (see shortfall against standard T1a).

Description of inspection activities undertaken

The inspection timetable was developed in consideration of the activities conducted under the licence, compliance update information and discussions with the DI. The inspection included review of the establishment's procedures for conducting activities under the licence and interviews with staff. The inspection also included a visual inspection of the areas where samples are stored under the licence and audits of sample traceability.

Traceability audits were conducted on samples in the following storage locations:

Samples stored at -80°C in the main building:

- two urine samples stored under ethical approval from a Research Ethics Committee (REC) from sample log to storage location;
- two swab samples from commercial suppliers from sample log to storage location;
- two urine samples stored since 2016 from storage to sample log.

Samples stored at -80°C in the external storage unit:

- Two boxes of urine samples from a longitudinal study (one donor per cryobox) from storage to sample log.

Samples stored at -20°C in the Class 2 laboratory:

- Two donor swabs from storage location to electronic storage record.

Major discrepancies were identified with the traceability of all samples stored at -80°C because exact storage locations were not recorded (see shortfall against standard T1c). Samples stored in the storage unit at -20°C showed full traceability from storage location to storage record.

Audits of consent forms for volunteer donors were also performed for completeness from the following studies:

- Study using saliva samples: from a total of 11 consent forms, boxes confirming consent on three forms were ticked and not initialled. No donor numbers were associated with the forms;
- Study using swab samples: all fully completed;
- Study using urine samples: from a total of 51 consent forms, boxes confirming consent on nine forms were ticked and not initialled;
- Study using blood samples: all fully completed;
- Blood glucose study: from a total of 16 consent forms, boxes confirming consent on two forms were ticked and not initialled. No donor numbers were associated with the forms.

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

Consent

Standard	Inspection findings	Level of shortfall
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the HTA's Codes 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.	Although the establishment has a consent SOP for clinical trials, there is no documented procedure for seeking consent from local donor volunteers with the requirements of the HT Act.	**Minor**
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.	The current consent form includes consent to use of the samples but not storage of the samples.	**Major**
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent		
c) Competency is assessed and maintained.	Although there is evidence of consent training, staff are not competency assessed and, at the time of the inspection, there was no evidence of refresher training.	**Minor**

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process		
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.	Although the establishment holds regular governance meetings, there was no minuted evidence of HTA related matters discussed at these meetings.	**Minor**
GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	The internal audits do not cover the full range of activities carried out by the establishment and are not against all applicable HTA standards.	**Minor**
GQ4 There is a systematic and planned approach to the management of records		
b) There are provisions for back-up / recovery in the event of loss of records.	The paper sample record log is electronically scanned bi-annually as a back-up. The paper sample record does not record the sample location in storage; this is recorded on the paper location map displayed on the freezer doors. The location map on the freezer door is not copied as a back-up and, in the event of loss of the map, the sample location cannot be identified.	**Major**

Traceability

Standard	Inspection findings	Level of shortfall
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.	The pseudonymised donor number was not recorded on the consent forms for two studies. The samples therefore cannot be linked to the donor in the case of potential withdrawal of consent.	**Minor**

b) A register of donated material, and the associated products where relevant, is maintained.	Although all samples are stored under the same governance arrangements, the establishment does not currently track expiry of REC approved projects and therefore are unaware when samples are stored under the HTA licence.	**Major**
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.	Although sample details are recorded in the sample log, storage locations are not recorded in the log and details of the exact sample storage locations are not recorded. The freezer number is not recorded in the sample storage log.	**Major**
T2 Bodies and human tissue are disposed of in an appropriate manner		
b) The date, reason for disposal and the method used are documented.	The method of disposal is not recorded in the sample storage record.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE1 The premises are secure and fit for purpose		
c) There are documented cleaning and decontamination procedures.	At the time of the inspection, there were no documented cleaning and decontamination procedures associated with storage of human tissue.	**Minor**
PFE2 There are appropriate facilities for the storage of bodies and human tissue		
c) Storage conditions are monitored, recorded and acted on when required.	There is an alarm call out system in place for storage at -80°C but not for the -20°C freezer in the Class 2 facility. The alarm call-out system is not challenge tested to ensure that the dial-out system, which notifies staff, is functioning properly. The temperature is currently monitored weekly but this data is not monitored for trends in temperature deviations over time.	**Major**
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.	The -80°C freezers storing human tissue are not currently under warranty and are not regularly maintained under a maintenance contract (see Advice, item 9)	**Minor**

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to add person(s) designated under the licence to ensure all activities are overseen under the licence in the absence of the DI.
2.	C1d	The DI is advised to include the contact details of the consent seeker in the consent form in the event that the donor wishes to withdraw consent.
3.	GQ1b	The DI is advised to consider labelling all storage units to indicate that they contain human tissue samples stored under the licence. This will also help to ensure that human and non-human samples are stored separately.
4.	GQ2a	The DI is advised to expand the scope of the audits to also include completeness of consent forms and more frequent traceability audits.
5.	GQ3a	The DI is advised to include ethics and consent training as a separate item in the individual agreed Training Plan and Record to ensure consent training is evidenced.
6.	GQ6a	The DI is advised to document in the risk assessments the full range of control measures in place, which help to mitigate identified risks to the storage of human tissue.
7.	T1a	The DI should ensure that when storing aliquots of the same sample with the same identifier, the unique storage location for each aliquot is recorded in the sample log to ensure full traceability from consent to use or disposal.
8.	PFE1b	The DI is advised to risk assess access to the storage unit where human tissue is stored together with other material stored by the establishment's manufacturing department as freezers storing human tissue are not locked.
9.	PFE3a	The DI is advised to risk assess the shortfall against standard PFE3a and to put in place the following: • Labelling of the freezers with the lower and upper alarm set point temperatures to alert staff to temperature excursions; • Labelling of the freezers to demonstrate that human tissue samples are stored under the HTA licence. The DI is advised to update the documented procedure, SOP 004, V3, Fridges and Freezers so that it reflects the procedures to be followed in relation to the points above.

Concluding comments

As this was the first full inspection for the establishment, the staff were very open to suggestions to improve practices to ensure compliance.

There are a number of areas of practice that require improvement, including five major and eight minor shortfalls. These were due to issues relating to weaknesses in the following areas: documented procedures for seeking consent from donor volunteers and refresher training for consent seekers, governance meetings, audit and record keeping, traceability systems and maintenance and monitoring of equipment.

The HTA requires the Designated Individual to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 24 July 2018

Report returned from DI: 24 July 2018

Final report issued: 1 August 2018

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: 8 August 2019

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.