Licence application assessment visit report on compliance with HTA licensing standards

Stemnovate Ltd.

Proposed HTA licensing number 12680

Application for a licence 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**

23 July 2018

Summary of inspection findings

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

Although Stemnovate Ltd (the establishment) was found to have met the majority of the HTA standards, one minor shortfall was found in relation to risk assessments.

The HTA has given the proposed DI advice with regards to some aspects of consent, governance and quality systems 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

Stemnovate Ltd (the establishment) is a start-up company developing novel technologies for modelling human disease. The establishment has applied for a HTA licence for storage of relevant material which has come from a human body for use for scheduled purposes. Human samples will be stored for use for the scheduled purpose of 'Research in connection with disorders, or the functioning, of the human body'.

Stemnovate Ltd is located in a multi-tenanted science building. The purpose-designed laboratory facility is secured by swipe card which can only be accessed by Stemnovate Ltd or facilities staff.

The establishment plans to acquire human samples including blood, skin biopsies and tissue (from living donors) through collaborators and commercial suppliers. Although the establishment will not be involved directly in obtaining consent, Stemnovate Ltd have produced consent forms and information sheets for collaborators to use and agreements are in place to ensure consent is obtained in accordance with the requirements of the HT Act and HTA's Codes of Practice (see *Advice,* item 1).

Samples will be sent to the establishment by tracked courier services. Relevant material will be anonymised and assigned a unique identification code to track sample receipt, storage, use, transport off site and disposal. The establishment will use paper forms and an electronic database to record details of sample traceability.

Samples will be stored at -80°C and in liquid nitrogen. There is a new temperature-controlled -80°C freezer in the main laboratory that is under manufacturer's warranty (see *Advice*, item 9). There are documented daily temperature records kept and it is connected to an automated alarm system to alert staff of deviations from the set acceptable temperature ranges, including a call-out notification procedure (see *Advice*, item 8). The liquid nitrogen tank is situated in a locked building adjacent to the Stemnovate Ltd laboratory and is covered by CCTV. Although several laboratories use the space, training is provided before access is granted and there is a lock on the liquid nitrogen tank holding relevant material. Filling and maintenance of the liquid nitrogen tank is provided by the site's facilities management team. The establishment has contingency arrangements for back-up, on-site, temperature-controlled storage, with available space in other monitored -80°C freezers and liquid nitrogen tanks.

Description of inspection activities undertaken

This report describes a licence application assessment site visit to assess the suitability of the establishment to hold a HTA licence. The suitability of the proposed DI, proposed Licence Holder and premises were assessed. The inspection included; review of the establishment's procedures for conducting activities under the licence; meetings with staff; visual inspection of

the areas where it is planned that samples will be stored; and a review of the sample traceability system that will be used.

Inspection findings

The HTA found the proposed Licence Holder, the proposed Designated Individual and the premises to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
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.	Although the establishment has a procedure for conducting risk assessments, there are no documented risk assessments of the risks associated with the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. *Refer to Advice, item 6.*	**Minor**

Advice

The HTA advises the proposed DI to consider the following to further improve practices.

No.	Standard	Advice
1.	C1(b)	Consent withdrawal is offered for 30 days after consent has been obtained. After this time the sample is anonymised and used in research. The consent form details the time limit but does not explain the reasoning behind it. The proposed DI is advised to explain the reason for the 30 day time limit on consent withdrawal.
2.	GQ1(a)	The proposed DI is advised to include page numbers on all documents, including, but not limited to; • Storage contingency plan SOP • Training manual • Audit schedule • Audit checklist • Risk assessments
3.	GQ1(d)	All staff working under the licence should be aware of the governance arrangements in place, and they should be represented at governance meetings. The proposed DI is advised to include a HTA standing agenda item

		in a relevant meeting. Minutes of governance meetings should be circulated to all relevant staff to help to ensure that they are aware of all important information relating to activities conducted under the licence.
4.	GQ2(a)	Audits against the old HTA standards are included in the audit schedule. The proposed DI is advised to update the 'Audit Checklist' document and audit against the current HTA standards (published April 2017).
5.	GQ3(a)	The proposed DI is advised to assure himself that all staff involved in undertaking licensed activities are aware of the requirements of the HT Act and the HTA's Codes of Practice. Training should be provided and refreshed as appropriate.
6.	GQ6(a)	To address the minor shortfall against standard GQ6(a), the proposed DI should ensure that documented risk assessments cover all of the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. In particular, the proposed DI should ensure that the following risks have been assessed: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; and • incorrect disposal. Further guidance on risk assessments of activities conducted under the licence can be found in the HTA's research sector licensing standards and guidance document, which is available on the HTA's website.
7.	T2(a)	The background section of the 'Disposal of Human Samples SOP' refers to the HTA's Code of Practice on Disposal. This is an old Code of Practice which has been updated and incorporated into the Code of Practice E on Research (published April 2017). The proposed DI is advised to modify this reference accordingly.
8.	PFE2(c)	The proposed DI is advised to implement formal tests of storage temperature alarms. This will help to ensure that the alarms are functioning as expected. The proposed DI is also advised to ensure that temperature records are monitored for trends. This may help staff to identify when storage conditions may be deteriorating and might alert staff to impending equipment failure.
9.	PFE3(a)	All equipment is new and under warranty. The proposed DI is to ensure that the freezers are subject to recommended calibration, validation and maintenance when the warranties expire.
10.	N/A	The establishment is currently expanding. The DI may wish to consider adding Persons Designated to the licence to provide greater support and oversight in relation to licensable activities. The HTA must be notified of any PDs.

Concluding comments

This report describes the licence application assessment visit of Stemnovate Ltd, which applied to be licensed under the HT Act for storage of relevant material which has come from a human body for use for scheduled purposes.

The HTA found the proposed DI and proposed Licence Holder to be suitable. Although the HTA found that Stemnovate Ltd had met the majority of the HTA's standards, one minor shortfall was found. 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 shortfall identified during the assessment.

Report sent to DI for factual accuracy: 20 August 2018

Report returned from DI: 28 August 2018

Final report issued: 28 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: 21 September 2018

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.