Site visit inspection report on compliance with HTA licensing standards

Unilever Colworth

HTA licensing number 12397

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**

30 October 2018

Summary of inspection findings

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.

Although the HTA found that Unilever Colworth (the establishment) had met the majority of the HTA's standards, one major shortfall and 11 minor shortfalls were found against a range of standards across the four main standards groups.

The DI has also been given advice on a range of issues and 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: C1lassification 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

This report refers to activities carried out by Unilever at the Colworth Science Park site in Bedford. The Designated Individual (DI) is a Team Leader within the Safety & Environmental Assurance Centre (SEAC), the Corporate Licence Holder (CLH) is Unilever and the Corporate Licence Holder contact (CLHc) is the Head of the Safety & Environmental Assurance Centre (SEAC) and the Colworth Site Leader for Unilever.

The establishment was granted a licence in November 2006 following an application in September 2006. The granted licence is in the HTA's research sector and is for 'storage of relevant material for use for a scheduled purpose which in this case is, 'Research in connection with disorders, or the functioning, of the human body'. There have been some changes to the DI, PDs and CLHc on the licence since it was granted.

The establishment is part of a major global company that supplies leading brands in personal care, household care and foods & refreshments. Unilever has many sites across the UK; however, the Colworth site houses several functions of Unilever's research and development groups.

At Colworth, two Unilever groups operate under this particular HTA licence; these are SEAC and the Beauty and Personal Care (B&PC) group. Due to a recent organisational change, many of the operations that previously took place at Colworth have since changed; this includes the B&PC group that was previously known as the Discover group. Both groups utilise human tissue for various projects, these are normally in collaboration with other Clinical Research Organisations who are contracted and sourced by Unilever.

The functionality of each group varies, SEAC have a global responsibility to generate safety risk assessment profiles, and generate safety data for Unilever. Using human tissue, SEAC generate models to look at metabolic competency and toxicological reactions to ensure the safety of Unilever products and processes. The B&PC group work to understand consumer needs and provide mechanistic understanding and screening for the Beauty and Personal Care function of Unilever.

The establishment have several different storage locations across the two departments, this includes three liquid nitrogen (LN2) dewers, with only one containing human tissue, that are stored in one of the labs accessed by staff. As well as this, there are several -80^{o}C freezers, a -150^{o}C freezer, a -20^{o}C freezer, room temperature storage and a +4^{o}C fridge. Some of the storage locations are monitored using external calibrated probes and weekly testing (see shortfall under PFE2(c)), others are monitored via the equipment's internal probe and external monitoring which goes to central security (see shortfall under PFE2(c)), the remainder are monitored using the equipment probe only.

The establishment uses tracking software, developed and installed specifically for their use. The establishment tracks the arrival, location and disposal of their samples; however, traceability discrepancies were found during the audit (see shortfall under T1 (b)). Some older collections are

held in paper-based workbooks, which pre-date the implementation of the tracker software (see shortfall under GQ4 (b)).

Description of inspection activities undertaken

The inspection was the second routine inspection of the establishment and consisted of a visual inspection, interviews with individual staff, traceability audits, document review and a roundtable discussion with establishment staff.

Traceability audits were completed on eight, randomly-selected samples across multiple different projects. Samples were selected from the -80ºC freezers, the LN2 dewers, the +4ºC fridge, the -20ºC freezer and the room temperature storage. At the time of the inspection, there was only one sample stored in the -150ºC freezer. Labels on the samples were noted and checked against the electronic records. Copies of the project consent forms were reviewed. There were discrepancies in two sets of traceability audits (see shortfalls under T1 (b) and (c)).

Inspection findings

The HTA found the LH, the DI 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.	The establishment does not have any procedure should a participant wish to withdraw their consent.	**Minor**
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.	The consent aspects, and the level of information provided to assure accordance with the requirements of the HT Act and the HTA's Codes of Practice, vary between material transfer agreements (MTAs). *See Advice, item 1.*	**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		
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.	There is a clear division in the governance frameworks between the two groups. B&PC operates under only two Standard Operating Procedure (SOP). Not all licensable activities are covered within the documentation. Areas that were missing included: • Receipt of samples. • Storage arrangements for samples. • Labelling of samples. *See Advice, item 3.*	**Minor**
c) There are change control mechanisms for the implementation of new operational procedures.	New or amended documents are not acknowledged as being read or understood by relevant staff. *See Advice, item 4.*	**Minor**
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.	The B&PC do not maintain training records or competency assessments.	**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.	Some vital records are being maintained in paper format, with no provision for back-up or recovery. *See Advice, item 5.*	**Minor**
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.	Whilst the establishment does have risk assessments, these are not robust enough and do not cover licensed activities. The current risk assessments do not cover all of the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. *See Advice, item 6.*	**Minor**

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		
b) A register of donated material, and the associated products where relevant, is maintained.	A number of concerning matters relating to this standard were found: • The sample tracking number was not always written on the sample. • There were inconsistencies in the information written on the samples. Some had their tracking numbers and others did not. • Whilst completing the audit using the tracking software, a sample was unintentionally moved when attempting to check its location. This change was not controlled or tracked in the sample history, and was easy to manipulate. • The information stored on the tracking software varies between projects. The curator or project lead records different information that is not universal or accessible to all staff. *See Advice, item 8.*	**Minor**
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.	During the audit, there were two sets of sample with discrepancies: either the location was incorrect, the sample could not be located in the tracking software or the information was not clear on either the sample or tracking software. *See Advice, item 9.*	**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.	There are currently no documented cleaning or decontamination procedures at the establishment.	**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.	Not all storage conditions are monitored and, for those that are, the current monitoring method is not sufficient or suitable. There are large gaps in the temperature monitoring, increasing the likelihood that temperature excursions go undetected. A number of concerning matters relating to this standard were found: • There is no documented procedure for what staff should do when there are temperature excursions. The establishment have an "Adverse Incidents" SOP; however, this does not detail the actions taken should there be a call out. • Staff are unaware of accepted temperature ranges of the storage equipment and are unaware of the reporting channels for any alarms or equipment issues. During the inspection, the battery indicator light was flashing on one of the freezer display panels. Both the DI and staff were unaware if this had been reported or when it had started to flash. • The establishment does monitor some of the storage equipment; however this is done once a week by one person and in some cases, only the minimum and maximum temperatures are recorded for an entire week period, without giving the exact date and time of the excursion or sounding an audible alarm. The above process means that there is no back up should that one person be unavailable and there is a risk that the equipment may be out of temperature range for a maximum of 6 days without staff being aware when or how long it has been out of range. • Not all storage conditions have external probes or audible alarms, therefore staff are unaware of excursions for a long period of time. The establishment relies on the internal probe on the inside of the door, which is subject to battery failure as well as temperature fluctuations when the door is opened. • For the equipment that is on an external alarm system, the system itself is not tested frequently, meaning that issues are only raised in the event of an alarm or when something is changed within the system.	**Major (Cumulative)**
d) There are documented contingency plans in place in case of failure in storage area.	There are no documented contingency arrangements in place.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1 (c)	In order to obtain consistent assurances about informed donor consent, the DI is advised to consider implementing a standardised MTA
2.	C1 (d)	The establishment receives samples from several sources, each study providing information to donors. The DI is advised to assure themselves that the information provided to donors is sufficient to ensure that informed consent has been obtained. Examples of this include assurances in relation to withdrawal of consent and the use of donated tissue, including how long it will be stored and who will access it.
3.	GQ1 (a)	The SEAC group is also regulated by the MHRA for GLP Compliance, while the B&PC group is not. This means that both groups are under a different governance framework. The DI is advised to consider aligning the governance frameworks to ensure that both groups are operating consistently in terms of regulatory compliance.
4.	GQ1 (c)	Currently, there is no process in place to ensure that changes to operational procedures are signed off and understood by relevant staff, particularly the recently developed SOP in relation to the HTA Licence, which replaced two previously separate SOPs. The DI is advised to implement a sign off procedure for the generation of new or updated SOPs.
5.	GQ4 (b)	Paper records for samples that predate the implementation of the software and equipment monitoring are kept, the DI is advised to back these up electronically,
6.	GQ6 (a)	The DI is advised that risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities, including: • receiving and/or storing specimens without appropriate • consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for • useful research; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment ; • security arrangements; • Incorrect disposal.
7.	T1 (a)	The DI is also advised to consider changing the practice of writing on the vials with pen as this could cause multiple problems, such as difficulties in reading label, smudging, limitations with space and difficulty correcting errors.
8.	T1 (b)	The DI is advised to consider whether a unified register may be kept rather than multiple different registers.

9.	T1 (c)	During the inspection, it was noted that the establishment had raised an issue with the date updating feature of the tracking software. The DI is advised to make sure this is fully documented, cascaded to all relevant staff and actioned as soon as possible.
10.	T2 (a)	The DI is advised to consider how disposing of samples from the deceased can be carried out in the most sensitive manner available. The HTA guidance recognises that what is sensitive and what is feasible at local level needs to be taken into account. It is good practice for human tissue to be bagged separately from clinical waste.
11.	PFE1 (a)	The establishment has three small liquid nitrogen dewers stored, in one of the labs; however, there are no oxygen depletion alarms. Although there is an alarm that can be worn by staff, there is only one available and staff continue to access and fill the liquid nitrogen when the personal alarm is not on site. During the time of the inspection, the personal alarm was off-site for servicing and staff continued to access the liquid nitrogen. The establishment has a carbon dioxide alarm; however, this appears to be mounted too high up on a wall. The establishment is advised to check this health and safety matter. The establishment staff regularly fill the liquid nitrogen themselves; however, this is not recorded anywhere. The DI is advised to consider whether the health and safety risks relating to this process are adequately mitigated.

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 DI has developed a comprehensive HTA training presentation that is presented to all staff rather than just those who use human tissue. In addition, re-training takes place every 2-3 years.

- The Corporate Licence Holder contact (CLHc) has a good level of engagement with the DI and PDs working under the licence, this means any issues can be raised and actioned within good time.

- The establishment has a good system for reporting and recording incidents relating to human tissue. Any incident is well documented and investigated promptly by staff.

- Both SEAC and B&PC are well represented on the licence, with multiple PDs on the licence from both groups. The PDs are within the HTA Committee and meet regularly with the DI.

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

Although the HTA found that Unilever Colworth (the establishment) had met the majority of the HTA's standards, one major shortfall and 11 minor shortfalls were found against a range of standards across the four main standards groups.

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: 21 November 2018

Report returned from DI: 26 November 2018

Final report issued: 27 November 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: 06 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.