Site visit inspection report on compliance with HTA licensing standards

University Hospital of Wales

HTA licensing number 12422

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**

24 - 26 September 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 University Hospital of Wales (the establishment) was found to have met the majority of the HTA standards, one minor and two major shortfalls were identified against the Consent and Traceability standards.

The DI has also been given advice on a number of areas. 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

This report refers to activities carried out at University Hospital of Wales (the establishment). The establishment is licensed for the storage of relevant material that has come from a human body for use in a scheduled purpose, under the Human Tissue Act 2004 (HT Act). Human samples are stored for use for the scheduled purpose of 'research in connection with disorders, or functioning, of the human body'.

The establishment has been licensed since July 2007 and this was the third routine site-visit inspection to assess whether it continues to meet the HTA's standards. All standards were found to be met in the previous inspection carried out in December 2015.

The licence covers the hub site at University Hospital of Wales (Heath Park), and a satellite premises, located in Cardiff University (Cathays Park). At the hub premises there are approximately 160 individual human tissue research projects within the Schools of Medicine, Dentistry and Healthcare Sciences as well as six research tissue banks (RTBs): Cardiff University Biobank (18/WA/0089), Archie Cochrane Biobank (15/WA/0368), Acute Myeloid Leukaemia RTB (13/WA/0058), Cardiff School of Dentistry tooth bank (17/WA/0405), Wales Kidney RTB (09/WSE02/48+5) and the Welsh Neuroscience RTB (12/WA/0073). At the satellite site, there are approximately 66 individual human tissue research projects held in the Schools of Biosciences, Medicine, Optometry and Vision Sciences, Pharmacy and Pharmaceutical Sciences and Psychology and one RTB (South Wales Initiative for Fetal Tissue (SWIFT) Research Tissue Bank (18/WA/0125).

Chief Investigators are directly responsible for the day to day running of the RTBs and projects, and Human Tissue Officers (HTOs) oversee compliance and monitor activity. Before all new projects are started, Chief Investigators are required to sign a declaration affirming that standards will be followed. There is at least one HTO within each school and all are named Persons Designated (PDs) on the licence. There is a clear reporting structure from the Chief Investigators to the HTOs (PDs) to the HT manager and the DI. The DI is the Dean of International and a Professor in Cell Biology and the Corporate Licence Holder contact is the College Pro-Vice Chancellor.

There are overarching governance documents across the individual projects and the RTBs which includes a Code of Practice and Standard Operating Procedures document that covers all main activities being carried out under the licence. There is a centralised 'Register of Tissue Holdings' listing all collections with details of the collection, persons responsible and location. The establishment has some projects that have approval from a recognised research ethics committee (REC) and are therefore exempt from the licensing requirements of the HT Act, however the establishment adopts a harmonised approach to governance and all studies are recorded on the centralised database.

There is a vast amount of samples held under the licence that have been obtained from both living and deceased donors. Samples include whole blood and blood components, teeth, peritoneal fluid, cerebrospinal fluid, saliva, placenta, urine and human tissue.

All storage areas are secured in designated laboratory areas. All freezers are fitted with automated alarms that are triggered by deviations from the set acceptable temperature ranges. Relevant staff are immediately alerted by email and text when alarms are triggered. Some of the alarm systems are challenged (see Advice, item 6). The room containing the liquid nitrogen storage tanks is secure and is fitted with an oxygen monitoring system. As well as back-up, the establishment has contingency arrangements for all temperature-controlled storage.

All of the RTBs stored under the licence have local SOPs in addition to the overarching ones (see Advice, items 3 and 5). For the samples in the RTBs, patients and volunteers are contacted and given relevant documentation including an information sheet. Once the participant agrees to take part, consent is sought by trained staff using an appropriate consent form. After samples are taken, they are given a unique identification number and patient files are anonymised. Each RTB has their own database that records the identification number and relevant sample details. The RTBs provide a resource for researchers and there is an application process including an assessment by a committee before samples are approved to be sent out for research.

For material stored under the licence for individual projects, there is a school ethics committee review of the project before material is obtained. Material is obtained by trained researchers themselves using a specific information sheet and consent form, or from other establishments with material transfer agreements in place including from overseas.

Description of inspection activities undertaken

The inspection timetable was developed in consideration of the activities conducted under the licence, compliance update information, discussions with the DI, communications with the HTA and the findings of the previous inspection. The inspection included review of the establishment's procedures for conducting activities under the licence and roundtable discussions with staff responsible for the RTBs and collections or projects. The inspection also included a visual inspection of the areas where samples are stored under the licence and audits of sample traceability. Audits of the following randomly selected samples were conducted:

- Five samples from the Cardiff School of Dentistry RTB were audited from record to sample. All samples were fully traceable.
- Ten samples from the Cardiff University Biobank were audited from record to sample, and sample to record. All samples were fully traceable.

- Four samples from the Archie Cochrane RTB were audited from sample to record. All samples were fully traceable although disposal records were incomplete for two samples (see Shortfall against standard T2(b)).
- Two samples from the Acute Myeloid Leukaemia RTB were audited from sample to record. Samples were not traceable (see Shortfall against standard T1(c)).
- Four sample records from the SWIFT RTB were audited against the traceability database. One sample record was not recorded on the database.
- Eight samples from the Wales Kidney RTB were audited from consent documentation to record to sample. All samples were fully traceable.
- Eight samples from the Welsh Neuroscience Research RTB were audited from sample to consent. All samples were fully traceable.
- Six individual projects were audited for disposal records, consent documentation and traceability. All samples were fully traceable although one collection had samples that were being stored beyond the consent duration that was agreed and one study had a number of consent forms that were incomplete (see Shortfall against standard C1(a)).

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

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 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.	Samples are being stored from an individual research project beyond the agreed duration of storage. The samples are from a REC approved project for which the approval has since expired. The consent form stipulates that the tissue will be stored for 'weeks' and the tissue has been stored since 2011. During the HTA audits for one of the individual projects, although consent had been given, three consent forms were incomplete, with the consent seeker's details, signature and date missing.	**Major**
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail		
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.	Discrepancies were identified in the audit trail of samples randomly chosen from two of the RTBs leading to the loss of traceability of relevant material. One sample that had arrived into the SWIFT RTB was not inputted onto the sample database. Two samples that were on the sample database for the Acute Myeloid Leukaemia RTB could not be located in the specified storage area.	**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 spreadsheet used by the Archie Cochrane RTB does not detail the date, reason and method of disposal for samples.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1(a)	The 'Records Management Policy' was last reviewed in June 2016. The DI is advised to ensure that all documents relevant to licensable activity are reviewed regularly.
2.	GQ1(a)	The SOP for 'The use or storage of human tissue for the purposes of research or education' (document 2CU/15/HTA19/3.0) references the old Code of Practice on import and export. The guidelines are now covered within the Code of Practice E (Research). The DI is advised to update this reference.
3.	GQ1(a)	The SWIFT RTB does not have a schedule of SOP review. The DI is advised to bring the SWIFT RTB into line with all other RTBs and ensure that their local SOPs are reviewed regularly.
4.	GQ2(a)	During the audit of consent forms for the individual reseach projects some of the check boxes had been ticked instead of being initialled as per instructions. Although the RTBs are audited annually, only a handful of the individual projects undergo auditing by the HT team each year. Auditing of all collections is recommended and the DI may wish to implement a more robust system of audit. The DI is advised to ensure that the audit schedule includes vertical audits of records and samples, from sample through to consent documentation. Records should be audited regularly to ensure completeness, accuracy and legibility.
5.	GQ6(a)	Each RTB has an independent risk assessment. Although hazards are documented, the liklehood scoring needs review. For example, the likelihood of the use of a sample with incorrect consent is scored at zero. The DI is advised to review the risk assessments for the Cardiff University Biobank, Archie Cochrane Biobank and Wales Kidney RTB and reassess the scoring.
6.	PFE2(c)	All of the temperature-monitored freezers have external alarm and call-out systems and some of the RTBs challenge these systems. The DI is advised to challenge all alarm systems to ensure that when temperature deviations are detected, the system operates successfully. The DI is also advised to review temperature trends.

Concluding comments

This report outlines the third, routine HTA site visit inspection of University Hospital of Wales. A number of strengths and areas of good practice were observed during the inspection, including:

- There is a large amount of activity taking place under the licence and the DI has developed a robust staff structure to ensure full oversight. Authority and responsibilities are shared between the HTA manager, HTA compliance team and HTOs (PDs). The responsibilities of individuals are clear and documented within the

establishment's Code of Practice.

- For the RTBs where issues were identified, the establishment are currently in the process of transferring them into the Cardiff University Biobank. The centralised governance will provide support and infrastructure to the RTBs, strengthening overall compliance.
- The Welsh Neuroscience Research RTB has developed an excellent in-house traceability system that is efficient and easy to use. It provides details of all 100,000 samples the bank holds, from consent forms to sample information and location.
- Staff at the establishment demonstrated that they strive towards improvement of practices, and were open to the advice offered by the HTA during the inspection.

Although there are areas of practice that require improvement, including one minor and two major shortfalls, 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.

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.

Report sent to DI for factual accuracy: 17 October 2018

Report returned from DI: 30 October 2018

Final report issued: 05 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: 01 March 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.