Site visit inspection report on compliance with HTA minimum standards

Almac Diagnostics

HTA licensing number 12559

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**

25 November 2014

Summary of inspection findings

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

Almac Diagnostics (the establishment) was found to have met all HTA standards.

Particular examples of strengths and good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual (DI), Licence Holder, premises and practices are suitable.

The statutory duties of the DI 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.

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. The HTA inspects the establishments it licences against four groups of standards:

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

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, 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 given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

The licensed establishment forms part of a larger commercial organisation with facilities in Northern Ireland, England and the United States of America. The establishment provides laboratory services to commercial partners and clients in the biopharmaceutical field, principally pharmaceutical companies, universities and hospitals involved in clinical trials. The services offered by the establishment include biomarker discovery, assay development and clinical trials management.

Research work is carried out on samples from living donors only, tissue samples mainly being in the form of formalin fixed paraffin embedded (FFPE) tissue blocks or slides, though other samples, including whole blood taken from volunteer staff members, are also used in research projects.

In many cases, samples are rendered acellular within a few days of receipt and thus do not fall into the remit of the HTA, but many projects carried out by the establishment involve longer term storage of relevant materials. Ethics approval may be by national or local committees, within the UK or abroad.

In advance of the start of each research project, client service agreements and material transfer agreements are put in place and these govern the nature of the work to be carried out by the establishment. The agreements also make provision with regard to consent

requirements, providing that consent procedures meet the requirements of local ethics approval or the Human Tissue Act. They also govern how samples which are not destroyed during assay or other work carried out are disposed of or returned to the client at the end of the project.

When research involves blood samples provided by staff volunteers, consent is taken by staff members, usually research project managers or senior scientists, trained in consent procedures for clinical trials as part of Good Clinical Practice (GCP) training. These staff members have also undertaken specific training on the requirements of the Human Tissue Act, carried out by the DI. Tailored consent forms and patient information leaflets are used for each project. To ensure anonymity of the samples supplied to the research team, signed consent forms are retained within a restricted area of the establishment, formerly the Occupational Health department, but now within the Quality Assurance department, under direct control of the DI. The use of unique participant numbers ensures confidentiality.

When anonymised samples are received from client organisations, trained laboratory staff reconcile the samples with the delivery manifest before logging the samples into the Laboratory Information Management System (LIMS). This initial manual entry is cross checked by a second member of staff to minimise risk of error. Any discrepancies at this stage are raised as a non-conformity and enquiry is made of the client. The LIMS then allocates each sample a unique identifier and any other samples derived from the “parent” sample are provided with further, barcoded, unique identifiers, ensuring traceability back to the original tissue supplied.

Storage of samples takes place in two areas of the establishment; the laboratory and cold room/archive, with storage being at ambient temperature, in refrigerators at 2 to 8 ºC, or freezers at -20 ºC or -80 ºC, depending on the nature of the tissue stored. Sample location is recorded within the LIMS, accessible by staff selecting samples for project work. All storage equipment is subject to regular maintenance and calibration and equipment is linked to on-line temperature monitoring with alarms. Temperature trends are monitored and as part of project review, the temperature records for samples used in clinical trial work are reviewed to ensure no out of specification temperatures have occurred.

The nature of the work carried out by the establishment often results in destruction of the samples, and this is recorded within the LIMS, as is disposal or return to the client at the end of each project. Where it occurs, disposal follows the establishment’s documented clinical waste procedure.

Samples returned to clients are inventoried in Clinical Sample Return Checklists, which are countersigned by a second member of staff. Dispatched samples are tracked by use of courier tracking systems, transport documentation is retained, and receipt is confirmed by email.

A similar procedure is used for samples sent elsewhere for specialist examination, for example to histopathologists, and strict protocols governing this ensure return of the samples within defined time limits.

This was the establishment’s first HTA inspection and comprised a visual inspection, review of governance documentation and records, and interviews with key staff.

An audit of traceability was carried out:

- Three imported samples were identified in the LIMS and the corresponding samples located within the storage refrigerator. The storage boxes were examined and the number of blocks or slides stored reconciled with the electronic record. The corresponding service or material transfer agreements were reviewed to confirm that appropriate consent had been obtained in line with local or Human Tissue Act requirements.

- One sample was located within another storage refrigerator and tracked back through the LIMS to confirm recorded location details.
- One sample was selected from the LIMS as the record showed it had been returned to the client organisation after project completion. The corresponding dispatch paperwork, including the Clinical Sample Return Checklist, was located.
- One blood sample was located within the storage refrigerator, details of location found on the LIMS system and the corresponding consent documentation reviewed.

No discrepancies were found. For the blood sample the consent form was retrospective, as the original signed consent form had been inadvertently destroyed along with some others. This had been discovered by the DI during an earlier audit and raised as an internal incident. Reference to this was recorded within the LIMS, as was the corrective and preventative action carried out, in this case re-obtaining consent.

For the sample returned to the client, while retrieving the Clinical Sample Return Checklist was straightforward, to link this to a courier dispatch notice required a search through email correspondence. Advice has been provided to aid traceability in this regard.

Inspection findings

The HTA found the DI and the Licence Holder to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	C1, C2	The DI is advised to provide information to staff volunteering as project participants on how samples will be disposed of in any research project, as part of consent documentation. This should clarify situations where samples may be destroyed by work carried out during the project, disposed of following the completion of the project or, where applicable and subject to consent, retained for future studies. This will help to ensure study participants are more fully informed regarding the use of donated samples.
2.	GQ1	While the HTA notes that licensable activity is discussed at various governance meetings within the establishment, the DI is advised to consider having periodic governance meetings specific to those activities falling under the HTA licence and involving those carrying out licensed activity. This will help ensure that the DI has an opportunity to share learning with all staff involved in HTA specific activity and will allow staff to have a greater understanding of the role each plays in relation to HTA licensed activity.

3.	GQ6	The DI is advised to record courier dispatch tracking numbers on the Clinical Sample Return Checklist in order to more easily link the traceability of sample numbers to the transport paperwork. This will aid traceability in the event there is any query regarding transported samples or in the event of an issue with the transport of samples which requires to be investigated.
4.	GQ8	The HTA notes that the procedures relating to the taking and recording of consent, and agreements for the carrying out of research projects on behalf of clients ensure that provision is in place for appropriate consent. These help to minimise the risk of samples being retained without appropriate consent. However, the risk of sample retention without appropriate consent, and the mitigating steps taken, have not been recorded or referred to in the documented risk assessments of other regulatory risks carried out by the establishment. The DI is advised to add this risk to the regulatory risk assessments carried out by the establishment annually or at the commencement of each project, in order to ensure that appropriate steps are taken to ensure appropriate consent is in place for each new project.
5.	D1	The DI is advised that he should consider disposal of the small number of samples currently being retained on the instructions of a client organisation which has now ceased to exist. The reasons for, and method of, disposal should be recorded. The DI is further advised to seek legal advice on the contractual consequences of disposal of the small number of samples retained following completion of a project and for which the client has not yet accepted return, contrary to the project service agreement.

Concluding comments

The HTA saw several examples of good practice during the inspection. All operational laboratory staff, including those involved in taking consent, receive training on the requirements of the Human Tissue Act in addition to that received on GCP.

Storage of samples is carefully monitored and the establishment has well considered contingency procedures, including the use of uninterrupted power supplies, back-up generators and additional contingency storage elsewhere on site. The temperature monitoring alarm system and call out is challenged monthly by creating an artificial out of limits temperature event.

Staff training is managed on-line with updated procedural and governance documentation automatically emailed to staff for review and sign-off. Training records are reviewed to ensure staff complete required training.

Specific risk assessments have been carried out in relation to materials held under the HTA licence, including potential risks during transport and storage, and advice has been provided to extend these.

The HTA has also given advice to the DI with respect to consent documentation, traceability records relating to transport, governance meetings and the disposal of samples held at the end of project work.

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

Report sent to DI for factual accuracy: 4 December 2014

Report returned from DI: 15 December 2014

Final report issued: 15 December 2014

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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management

committees, agendas and minutes

- Complaints system

GQ2 There is a documented system of quality management and audit

- A document control system, covering all documented policies and standard operating procedures (SOPs).
- Schedule of audits
- Change control mechanisms for the implementation of new operational procedures

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills

- Qualifications of staff and training are recorded, records showing attendance at training
- Orientation and induction programmes
- Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training
- Training and reference manuals
- Staff appraisal / review records and personal development plans are in place

GQ4 There is a systematic and planned approach to the management of records

- Documented procedures for the creation, amendment, retention and destruction of records
- Regular audit of record content to check for completeness, legibility and accuracy
- Back-up / recovery facility in the event of loss of records
- Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ5 There are documented procedures for distribution of body parts, tissues or cells

- A process is in place to review the release of relevant material to other organisations
- An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail

- There is an identification system which assigns a unique code to each donation and to each of the products associated with it
- An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom

GQ7 There are systems to ensure that all adverse events are investigated promptly

- Corrective and preventive actions are taken where necessary and improvements in practice are made
- System to receive and distribute national and local information (e.g. HTA communications)

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately

- Documented risk assessments for all practices and processes
- Risk assessments are reviewed when appropriate
- Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards

PFE1 The premises are fit for purpose

- A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose
- Policies in place to review and maintain the safety of staff, authorised visitors and students
- The premises have sufficient space for procedures to be carried out safely and efficiently
- Policies are in place to ensure that the premises are secure and confidentiality is maintained

PFE 2 Environmental controls are in place to avoid potential contamination

- Documented cleaning and decontamination procedures
- Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination
- Appropriate health and safety controls are in place

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.

- Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination
- Contingency plans are in place in case of failure in storage area
- Critical storage conditions are monitored and recorded
- System to deal with emergencies on 24 hour basis
- Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination

- Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation
- A system is in place to ensure that traceability of relevant material is maintained during transport
- Records of transportation and delivery
- Records are kept of any agreements with recipients of relevant material
- Records are kept of any agreements with courier or transport companies

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored

- Records of calibration, validation and maintenance, including any agreements with maintenance companies
- Users have access to instructions for equipment and receive training in use and maintenance where appropriate
- Staff aware of how to report an equipment problem
- Contingency plan for equipment failure

Disposal Standards

D1 There is a clear and sensitive policy for disposing of human organs and tissue

- Documented disposal policy
- Policy is made available to the public
- Compliance with health and safety recommendations

D2 The reason for disposal and the methods used are carefully documented

- Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal
- Where applicable, disposal arrangements reflect specified wishes

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.