Site visit inspection report on compliance with HTA minimum standards

Alder Hey Children's Hospital

HTA licensing number 22595

Licensed for the

- **procurement of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007**

30 November 2017

Summary of inspection findings

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

Although the HTA found that Alder Hey Children's Hospital (the establishment) had met the majority of the HTA standards, four shortfalls were found in relation to the Governance and Quality System standards. The minor shortfalls relate to independent audits, the testing of donors, risk assessments and agreements.

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, Licence Holder, premises and practices are suitable.

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.

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.

Licensable activities carried out by the establishment

"E" = Establishment is licensed to carry out this activity.

Tissue category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell Haematopoietic, PBSC; PBSC	**E**						

Background to the establishment and description of inspection activities undertaken

Alder Hey Children's Hospital has been licensed by the HTA since 2009 and has recently applied for JACIE accreditation (Joint Accreditation Committee ISCT (International Society for Cellular Therapy). The HTA licence covers the procurement of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. The licensable activities undertaken at this establishment relate to peripheral blood stem cell (PBSC) collections from paediatric donors procured for autologous patient treatment. The establishment has not undertaken bone marrow procurement since the last HTA inspection.

Alder Hey Children's Hospital performs approximately five to six PBSC procurements each year. Consultant oncologists identify patients as potential candidates for a stem cell transplant procedure and seek consent from children or from parents (if the children are not competent to give consent). Consent discussions cover the apheresis procedure, insertion of vas-cath (when required), mandatory serology testing, storage, disposal of PBSCs (if required), chemotherapy and subsequent re-infusion of the cells. Blood samples for the mandatory serology testing are taken on the day of the consent and no earlier than 30 days before procurement of stem cells. Stem Cell Transplant Clinical Nurse Specialists at Alder Hey Children's Hospital also follow the patients throughout their treatment and provide support and age-appropriate patient and family information. Patients are given the opportunity during this process to discuss their treatment plan.

Following stem cell mobilization, CD34 counts are monitored before the patients are scheduled for apheresis. PBSC procurement takes place at the ward at Alder Hey Children's Hospital and is supported by specialist apheresis nurses employed by another licensed establishment. This establishment in addition to staff also provides equipment and consumables under the terms of an agreement (see *Advice*, item 2). Clinical staff based at the hospital are present when apheresis takes place. Harvested cells are transported to a second establishment (see *shortfall under GQ1(p)*). The second establishment is JACIE accredited and undertakes donor serology testing, processing, cryostorage and distribution for end-use of cells procured at Alder Hey Children's Hospital, under the terms of a service level agreement (SLA).

Transplantation takes place at Alder Hey Children's Hospital and staff from the second establishment transport the cryopreserved cells for re-infusion. They also bring a water bath and are responsible for thawing the cells before they are infused into patients in the presence of clinical staff at Alder Hey Children's Hospital.

This report describes the establishment's fifth routine inspection, which took place on 30 November 2017. Discussions were held with the Designated Individual (DI), the Programme Director, the Stem Cell Transplant Clinical Nurse Specialist and the Quality Manager. A review of documentation relevant to the establishment's licensable activities and a visual inspection of the premises where tissue procurement takes place, were also included as part of the inspection.

An audit was performed on three sets of patient records. The audit covered the documentation provided to patients who require autologous transplant at Alder Hey. The

donor name, date of birth, unique harvest number and hospital number, was cross-referenced, where applicable, against the consent to collect (see *Advice*, item 1), the consent for the testing, storage and discard of PBSCs, the stem cell consent for chemotherapy and stem cell transplant, harvest date, the serology results and re-infusion date. Traceability was maintained throughout. One discrepancy was identified in the accompanying documentation for one of the patient records related to the donor testing (see *shortfall under GQ5(b*)). A review was undertaken of the Quality Manual, key standard operating procedures, training records and agreements.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.	Although the establishment has agreements in place, these are not adequately clear about which establishment is responsible for the distribution of the PBSCs for processing following procurement.	**Minor**
GQ2 There is a documented system of quality management and audit.		
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.	No independent audit against all applicable HTA standards has been undertaken since the last HTA inspection. *Prior to the inspection, the establishment arranged for an independent audit to be undertaken by the Quality and Governance Medicine Division of the Trust.*	**Minor**

GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.	During the review of patient records, it was noted that on one occasion syphilis testing was not performed as part of the mandatory serology testing of donors.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
a) There are documented risk assessments for all practices and processes.	Although the establishment has carried out a number of risk assessments relating to licensable activities, recent changes to the establishment's IT systems were not adequately assessed prior to implementation.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1(e)	The establishment provides age-appropriate information leaflets to paediatric patients and their families before obtaining donor consent for the collection, testing, storage and possible discard of the cells. Current practice is for the staff from another licensed establishment to reconfirm consent on the day of the procurement and collect the consent form for the collection of stem cells for their records. The DI is advised to include a copy of the completed consent form for the collection of stem cells in the patient records.
2.	GQ1(r)	The DI is advised to review the agreement for the provision and transportation of the apheresis machine and the consumables to ensure the roles and responsibilities of each establishment are more clearly defined. For example, consideration should be given to the retention of raw data for 10 years after the use, expiry date or disposal of the PBSCs.
3.	GQ1(s)	The establishment has documented procedures for managing and recording serious adverse events and reactions (SAEARS) and a SLA with the second establishment that provides the processing, testing, storage and distribution of the PBSCs for end use. Both establishments are HTA licensed and the SLA specifies that any serious adverse events and reactions (SAEARs) are to be reported to the HTA within 24 hours.

		The DI is advised to further specify within the SLA the reporting requirements for any SAEARs as it is not clear which establishment would be responsible for reporting to the HTA within 24 hours of the incident.
4.	GQ2(b)	During the review of the establishment's audit of case notes it was noted that tick boxes and the date on the form were left blank. Clarity on how this audit is performed will assure the DI of its rigour, and enable other staff to perform such audits in the future. The DI is also advised to review the format of the form to ensure there are no sections that should be omitted.
5.	GQ2(c)	With reference to shortfall against GQ2(c), the DI is advised to ensure the independent audit is against all applicable HTA standards and takes place in the intervening year between HTA inspections.
6.	GQ3(b)	The establishment undertakes induction training for new members of staff. The training includes using the Peripheral Blood Stem Cell Harvest Checklist for Auto Transplant guide form, which lists the steps in the procedure. The DI is advised to formalise this procedure for new members of staff - • mention the Autologous Stem Cell Transplant guide form as part of the training provided, • ensure that the form is a controlled document, • include a formal competency assessment, • include a formal sign off process. Existing members of staff should have formal competency assessments.
7.	GQ5(b)	With reference to the shortfall against GQ5(a), the establishment requests a standard panel of donor tests. However, not all consent forms, literature provided to donors and SOPs refer to all mandatory tests. Examples include: • The consent for the testing, storage and discard form does not include HTLV 1/2 testing. • The Autologous Stem Cell Transplant Guide form does not include syphilis testing. • Standard operating procedure SCT/SOPB1 only includes HIV testing. The DI is advised to review the documentation and include all the mandatory serology tests.
8.	GQ8(a)	Although donor testing is carried out under the authority of another licensed establishment, the DI is advised to review the full range of control measures in place, which help to mitigate the risk that bloods for the mandatory serology testing are not obtained within the appropriate timeframes.
9.	N/A	The establishment has recently introduced a new proprietary software for document control and undergone various electronic system updates. The DI is advised to apply the principles of change management and document how these software changes have been implemented and

		embedded into the existing systems, including how information has been archived and retained by the Trust and how this will be made available to members of staff who need to access it.

Concluding comments

The HTA observed a number of good practices during the course of the inspection. There is a comprehensive and effective system of communication with weekly meetings for all members of staff in the apheresis unit and monthly meetings attended by representatives of the two establishments, with which Alder Hey Children's Hospital has agreements. Seminar-based learning takes place during the weekly meeting held in the apheresis unit.

Establishment staff have developed a communications book for their own use. This book provides information on new and existing patients including information on relapse and progression, radiotherapy and chemotherapy treatments and any updates from the weekly meetings. The communications book is a useful tool and ensures that the procedures remain effective and that all members of staff are aware of any new developments.

Patients and their families can attend the clinic discussion to ensure that they receive complete information and better understand the treatment plan and progress in treatment. Furthermore, a comprehensive summary of the discussion and outcomes is sent to the patients and their families, which evidences staff commitment to providing a high quality transplant service to their patients.

The establishment also routinely makes use of two-person check procedures for harvest identification, labeling procedures and re-infusion of the cryopreserved cells.

There are a number of areas of practice that require improvement, including four minor shortfalls. The HTA has given advice to the Designated Individual with respect to the consent forms, the agreements, the reporting of SAEARs, the internal and independent audits, the training of members of staff, donor testing, the risk assessments and the implementation of new software.

The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan 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: 08 January 2018

Report returned from DI: 22 January 2018

Final report issued: 25 January 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: 30 November 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.

Human Tissue (Quality and Safety for Human Application) Regulations 2007 Standards

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.
GQ2 There is a documented system of quality management and audit.
a) There is a quality management system which ensures continuous and systematic improvement.
b) There is an internal audit system for all licensable activities.
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.
a) There are clearly documented job descriptions for all staff.
b) There are orientation and induction programmes for new staff.
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.
d) There is annual documented mandatory training (e.g. health and safety and fire).

e) Personnel are trained in all tasks relevant to their work and their competence is recorded.
f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.
h) There is a system of staff appraisal.
i) Where appropriate, staff are registered with a professional or statutory body.
j) There are training and reference manuals available.
k) The establishment is sufficiently staffed to carry out its activities.
GQ4 There is a systematic and planned approach to the management of records.
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
d) There is a system for back-up / recovery in the event of loss of computerised records.
f) There are procedures to ensure that donor documentation, as specified by Directions 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 003/2010 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 003/2010.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.

GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.

PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
b) There are systems to deal with emergencies on a 24 hour basis.
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.
j) For each critical process, the materials, equipment and personnel are identified and documented.
k) There are contingency plans for equipment failure.

Disposal

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.
c) There is a documented procedure on disposal which ensures that there is no cross contamination.
D2 The reasons for disposal and the methods used are carefully documented.
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.

Appendix 2: Classification of the level of shortfall (HA)

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.

- **Critical shortfall:**

A shortfall which poses a significant direct risk of causing harm to a recipient patient or to a living donor,

Or

A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

A critical shortfall may result in one or more of the following:

- A notice of proposal being issued to revoke the licence
- 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.
- A notice of suspension of licensable activities
- Additional conditions being proposed
- Directions being issued requiring specific action to be taken straightaway

- **Major shortfall:**

A non-critical shortfall.

A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

or

A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

or

A shortfall which indicates a major deviation from the **Human Tissue (Quality and Safety for Human Application) Regulations 2007** or the **HTA Directions**;

or

A shortfall which indicates a failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

or

A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

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.

- **Minor shortfall:**

  A shortfall which cannot be classified as either critical or major and, which can be addressed by further development by the establishment.

  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 review or at the time of the next inspection.

  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.