Site visit inspection report on compliance with HTA minimum standards

JnJ Medical

HTA licensing number 22647

Licensed for the

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

11 January 2017

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.

JnJ Medical (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, 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.

'TPA' = Third party agreement; the establishment is licensed for this activity but another establishment (unlicensed) carries out the activity on their behalf.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Demineralised bone matrix (DBM)				**E**	**E**		
Acellular bone chips				**E**	**E**		

Background to the establishment and description of inspection activities undertaken

This report refers to the activities undertaken by JnJ Medical. The establishment is licensed for the storage and distribution of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations 2007). The establishment is located at Tingley, Leeds.

All the material is procured from deceased donors and processed at a tissue bank based in the United States of America (USA). The US tissue bank is accredited by the American Association of Tissue Banks (AATB) and carries out the mandatory testing of all the donors in accordance with the European Union Tissues and Cells Directives (EUTCDs). The European hub for JnJ Medical in the Netherlands imports the products from the USA and is responsible for ensuring that they meet equivalent standards for quality and safety as set out in the EUTCDs. This aspect of activities was not reviewed by the HTA, as it is regulated by the competent authority (CA) in that country. As the European hub, they are responsible for the subsequent distribution of the products to the UK and the rest of Europe by international couriers. The logistics headquarters of JnJ Medical is located in Belgium.

The staff at JnJ Medical undertake visual checks of packaging before they scan the products and add them to the inventory ready for distribution. The products are tracked as a batch, using a batch ID number provided by the US tissue bank. Each batch number can be traced back to the same donor, but each item does not have a unique individual serial number. The

warehouse where the products are stored is temperature-monitored. Any product with a shelf life of seven months or less is sent to the Netherlands and from there to the US establishment for disposal.

The establishment has been licensed by the HTA since 2013 and has been inspected on one previous occasion. This report describes the establishment's second routine site visit inspection, which took place on 11 January 2017. The inspection comprised of a visual inspection of the storage area, traceability audits, document review and interviews with key members of staff. The responsible person from the establishment in the Netherlands was also available for interview during the inspection.

The HTA visual inspection included the in-bound and out-bound areas, the storage area for demineralised bone products, the packing area and an inventory cage within the warehouse where non-conforming, damaged or with a short shelf life DBM products were stored before being sent for disposal.

The traceability audit of three products on a storage shelf, one product released for end use and one product sent for disposal, was undertaken. Order requests, storage locations, transport details, including distribution to end users or disposal records, were checked against electronic records. The training records of representative members of staff who handled the products were also checked. No discrepancies were identified.

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

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.	GQ4k	The establishment includes an Instructions For Use (IFU) information sheet for DBM products and acellular bone chips released for use. The IFU sets out the requirements for data retention and SAEARs reporting in relation to human tissue goods for "end users and/or distributors" of the products. The DI is advised to include in the requirements set out in the IFU that establishments that receive and intend to distribute products to other end users must hold an HTA licence as required by the Human Tissue (Quality and Safety for Human Application) Regulations 2007.
2.	GQ4k	The intra-company quality agreement between the logistics headquarters in Belgium and the operating companies includes a section, which references the quality and regulatory requirements and relevant legislation. Although the agreement lists appropriate legislation, including a reference to the Q&S Regulations 2007, it does not include reference to the EUTCDs.

		The DI is advised to include a reference to the EUTCDs in this agreement to ensure products imported meet all the necessary quality and safety requirements.
3.	GQ7a	The establishment has in place procedures for the identification, reporting, investigation and recording of serious adverse events and reactions (SAEARs), which reflect the fact that SAEARs may arise through the distribution of faulty or expired products or as a result of other product-related issues. The DI is advised to ensure, through SOPs and training that staff are aware that SAEARs may also arise through operational issues, such as the wrong product being sent to a customer resulting in cancellation or postponing of the patient's medical procedure. Such incidents should also be reported to the HTA.
4.	GQ8a	The establishment has carried out a number of risk assessments covering activities such as the storage and distribution of human tissue. The DI is advised to document the full range of control measures in place, which help to mitigate identified risks. This will help ensure that the impact on risk is appropriately reassessed when working practices or the facilities change. The DI is also advised to consider expanding the scope of the risk assessments to include the security of, and access to, the premises to ensure all of the risks are identified and appropriately assessed.
5.	PFE3c	The establishment uses a calibrated min/max temperature probe to monitor the air temperature where tissue and cell products are stored. Staff review the temperature data and are aware when the temperature deviates from the set values (15-25°C). The label on each product states simply that it should be stored at ambient temperature. However, the definition of ambient temperature is not set out in any of the establishment's documents or the IFU sheet. The DI is advised to obtain information from the supplier in the Netherlands and/or the US about the acceptable temperature range for products and the effect of temperature excursions on the quality and safety of these products, while in storage or during distribution. **Following the inspection the DI provided the temperature range for storage and shipping of the products based on the validation data of the manufacturer.**

Concluding comments

The HTA observed a number of good practices during the course of the inspection. The establishment has good training records both for permanent and temporary staff, which reflect a comprehensive system that helps ensure temporary staff are suitably trained before they undertake tasks.

Activities are supported by well-written documents, which are uploaded and managed using an electronic document system. The document system emails staff when there is a change to any documents, so that they can access the relevant documents and keep abreast of changes to practices and processes. There is a comprehensive audit schedule and effective systems of communication with monthly- and six-monthly meetings.

Products are stored in separate areas of the warehouse depending on whether the product is to be distributed to end users, received as part of a recall, or if the product is marked for

disposal. This practice ensures products marked for disposal or recall are not mixed up with products stored for release. At the packing area, staff print the IFU sheet immediately before they place it in the final package. This ensures that staff always send the most recent version of the sheet to end users.

The inspection team also noted a commitment on behalf of the establishment to deal with complaints and escalate if needed to the franchise in the Netherlands or the logistical support in Belgium.

The HTA has given advice to the Designated Individual in relation to a number of practices and procedures. This includes advice relating to the content of the establishment's information sheet sent out to end users, the intra-company Quality Agreement, risk assessments and SAEARs.

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

Report sent to DI for factual accuracy: 08 January 2017

Report returned from DI: 08 January 2017

Final report Issued: 09 January 2017

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

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.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
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.
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.
e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
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.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 003/2010.

l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
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.
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.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
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.
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.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.
b) There are systems to deal with emergencies on a 24 hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.

h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.
a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained.
f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.
i) Staff are aware of how to report an equipment problem.
j) For each critical process, the materials, equipment and personnel are identified and documented.

Disposal

Standard
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.

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.

1. **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:

   (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.

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.

3. 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.