**Site visit inspection report on compliance with HTA minimum standards**

**BioHorizons UK**

**HTA licensing number 11008**

**Licensed for the**

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

**6 January 2015**

## 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.

Although the HTA found that BioHorizons UK (the establishment) had met the majority of the HTA standards, one minor shortfall was found in relation to the primary labelling of the tissue products.

This was the establishment's fourth routine HTA inspection and since the last inspection, staff have continued to review and improve their practices. 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 type | Procurement | Processing | Testing | Storage | Distribution | Import | Export |
|---|---|---|---|---|---|---|---|
| **Bone chips** | | | | **E** | **E** | **E** | **E** |
| **DBM** | | | | **E** | **E** | **E** | **E** |
| **Mineralized cancellous bone particles** | | | | **E** | **E** | **E** | **E** |
| **Whole skin** | | | | **E** | **E** | **E** | **E** |

### Background to the establishment and description of inspection activities undertaken

BioHorizons UK is the UK-based branch of the American BioHorizons parent company, and is licensed for the import/export, storage and distribution of acellular products. The acellular material is purchased from American-based suppliers that carry out the donor selection, procurement, processing and testing of the tissue. BioHorizons US then exports the acellular material to BioHorizons UK for distribution or export to end users. Should any product become damaged or pass its expiry date, it is returned to BioHorizons US for disposal. The acellular products currently supplied are demineralised bone matrix (DBM), bone chips, mineralized cortical and cancellous bone particles and whole skin.

This was the establishment's fourth routine inspection, with previous inspections in 2009, 2011 and 2013. The inspection comprised a visual inspection, in particular of the storage area for the acellular tissue products, interviews with members of staff, review of relevant documentation and audits of the tissue products and associated records. An audit was conducted on the bone chips to verify the number of products on the database was the same as the number on the shelf, with checks made on lot numbers and expiry dates.

Three whole skin products of varying sizes were selected at random and the data for lot number, expiry date and receipt of the sample were compared with those on the database. No anomalies were found and all samples were stored in accordance with the storage instructions on their packaging. No samples were held in quarantine and samples nearing their expiry date were separated and clearly labelled. The inspection team noted that not all samples are labelled with the establishment's details and this is described further in the minor shortfall below.

## 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

### Premises, Facilities and Equipment

| Standard | Inspection findings | Level of shortfall |
|---|---|---|
| PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination. | | |
| i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions. | The Directions 003/2010 require that the primary tissues or cells containers must contain the identification of the tissue establishment or distributor in the UK. If this is not possible, a separate sheet can be used but this must be packaged in a manner that ensures they remain together (Guide to Quality and Safety for Human Tissues and Cells for Patient treatment paragraphs 159-160).<br><br>Whilst some of the products distributed under the licence have a sticker that provides details of the BioHorizons US parent company details, this is not strictly in keeping with the requirements, and others do not have this additional label due to the physical constraints of the size of the container. All products are distributed with paperwork of the order details which does include the information required by the Directions, but this is likely to become separated from the tissue products when they are unpacked by the end user and therefore the immediate link to the distributor, if there were a serious adverse event or reaction to report, will be lost. | **Minor** |

## Advice

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

| No. | Standard | Advice |
|---|---|---|
| 1. | GQ1b | Some of the establishment's procedural documents still refer to the previous address of the company. The DI is advised to ensure this is updated to the current address when these documents are next reviewed and may wish to consider omitting the address from these documents unless it is pertinent to the content.<br><br>When procedures were described to the inspection team, some areas of good practice were identified, such as routine double checks of contracts with end users before samples are distributed to them and photocopying the lot number on sample packaging, so there is a clear record of what samples were packaged to fulfil each order. However, the written documents for these procedures did not include this level of detail. The DI is advised to ensure all these areas of good practice are incorporated into the relevant documents to ensure consistency between staff carrying out the procedure. |
| 2. | GQ1k | Some of the products distributed to the end user may be returned to the establishment for resale providing they are returned within ten days of receipt and the end user confirms they have been stored in line with the storage requirements on the packaging. The DI is advised to make the contract, and any other information about returning products, more explicit to the end user about the requirement to store tissue products appropriately and the need for temperature monitoring. This will help to ensure that the end user is able to demonstrate that the products have been stored in accordance with the required quality and safety standards, should they wish to return them. |
| 3. | GQ2b | Audits of the establishment's processes are carried out, but are not very frequent. The DI is advised to implement more internal procedural audits to ensure staff compliance with procedures and also ensure procedural documents continue to reflect current best practice. |
| 4. | GQ5b | Audits of suppliers in the US are conducted by the parent company to ensure compliance with the European Directives. On review of the checklist used for these audits, the HTA advises that there should be more detail regarding the testing requirements, specifically in terms of what tests must be carried out and within what timescales. This will ensure that auditors are very clear on what the requirements are and ensure consistency of what is reviewed.<br><br>In addition, the DI is advised to ensure that any references to Directions 001/2006 within the establishment's documents are replaced with Directions 003/2010 which has superceded the aforementioned. |
| 5. | GQ2d | When audits of the suppliers of the acellular tissues are performed by staff at the parent company, the highlights of these audits are reported onwards. The DI is advised to ensure they receive copies of the full audit report to ensure that they are kept informed of any smaller issues that may have a bearing on their licensable activity. |

## Concluding comments

Since the last inspection, the establishment has continued to review and improve its practices and has met almost all of the licensing standards, with a number of areas of good practice as noted below.

There is a strong working relationship with the parent company in the US, to the extent that a member of staff travels to the establishment on a biannual basis to perform audits and conducts these from a distance in the intervening years. These audits are planned to coincide with the HTA inspection and therefore a member of staff from the US was present on the day and provided useful information on the US tissue suppliers and the audits that are conducted on them. Traceability audits are carried out weekly, where the US team sends a product type and the establishment has to respond with the number and details of the stock it holds. The US team checks these details against its records, and the database used by both teams,to ensure they are all in agreement.

The establishment has a thorough procedure for the release of products nearing their expiry date. These are normally only used when the product is otherwise out of stock and is required by the end user urgently. The end user is required to confirm acceptance of the expiry date before the product will be distributed to them.

The establishment has a good system of temperature monitoring for stored tissue products, whereby both maximum and minimum temperatures are monitored to ensure the products stay within the correct temperature range. The establishment has also sought supporting documentation from its suppliers regarding the temporary deviation of storage temperatures from their specified range, to ensure that over short periods, such as overnight transportation, this will not have an adverse effect on the quality or safety of the product.

There is one area of practice that requires improvement, which has been recorded as a minor shortfall. The HTA has also given advice to the Designated Individual with respect to audits and small changes to documentation.

The HTA requires that the Designated Individual addresses the shortfall 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 shortfall identified during the inspection.

**Report sent to DI for factual accuracy:** 11/02/15

**Report returned from DI:** 26/02/15

**Final report issued:** 02/03/15

**Inspection CAPA Plan Closure Statement:**

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: 23 April 2015**

## 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** |
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| 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. |
| i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded. |
| 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. |
| m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request. |
| n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 003/2010. |
| o) There is a complaints system in place. |
| 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. |

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| d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results. |
| 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. |
| g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010. |
| 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. |

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| 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. |
| 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. |
| 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. |
| e) Testing of donor samples is carried out using CE marked diagnostic tests. |
| 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. |

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| 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. |
| d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells. |

**Premises, Facilities and Equipment**

| **Standard** |
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| 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. |
| 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. |
| 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. |
| 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. |
| a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 003/2010. |
| 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. |

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| 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. |
| j) Shipping 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. |
| c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions. |

## 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.