Site visit inspection report on compliance with HTA licensing standards

ProImmune Ltd

HTA licensing number 12588

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**

26 September 2017

Summary of inspection findings

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

ProImmune Ltd (the establishment) was found to have met all the HTA standards.

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

The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and

- the conditions of the licence are complied with.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. They are grouped under four headings:

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

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, the level of the shortfall is classified as ‘Critical’, ‘Major’ or ‘Minor’ (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is provided.

HTA inspection reports are published on the HTA’s website.

Background to the establishment

This report refers to the activities carried out by ProImmune Ltd (the establishment). This was the second site visit inspection of the establishment since it was issued a licence in September 2011. It was a routine site inspection visit to assess whether the establishment is meeting the HTA's standards.

ProImmune Ltd is a private limited company, founded in 2000. It has approximately 25 employees, mainly at the Oxford site, and is a contract research organisation (CRO). The establishment offers solutions for preclinical and clinical immunology research, including antigen characterisation and products and services for tracking antigen-specific immune responses. The establishment works with over 500 organisations globally in the pharmaceutical, biotech, clinical research, government and academic sectors. Some research undertaken by the establishment involves the analysis of samples derived from clinical trials which are under United Kingdom Committee Authority (UKECA) approval and are exempt from the HTA's licensing requirements.

Relevant material (from the living) is stored for the scheduled purpose of: research in connection with disorders, or the functioning, of the human body ('research').

Tissue is supplied to ProImmune Ltd from sources both within and outside the UK. Each supplier provides confirmation that informed consent has been sought as part of a material transfer agreement (MTA). Relevant material stored under the HTA licence is primarily cellular preparations isolated from blood products, plasma samples and blood donations from healthy volunteer donors. Volunteer blood donations include those from specifically recruited volunteer donors as part of a blood donation volunteer register. Donors are contacted by email with a donor information sheet with details of the study. They are asked to self-certify that they are healthy and that blood has not been donated within the previous 12 weeks (if male) and 16 weeks (if female). After consent has been obtained by trained ProImmune staff, blood is taken by trained phlebotomists. Consent can be withdrawn at any time prior to the use of the sample. Consent is sought before each donation. All samples are de-identified and hard copies of consent forms are eventually converted to electronic form with appropriate backup by the Person Designated (PD). At the time of inspection, there were no donor samples stored.

Each donor blood sample is given a unique identifier and logged onto the sample tracking system database, which is backed up. This database tracks the sample from receipt into storage to disposal (see *Advice*, item 3). Donor blood samples are processed within 24 hours. The resultant plasma is then stored in a dedicated freezer. Samples sourced from suppliers are pooled donations and retain the original labelling (the lot number) as a sample identifier and are not relabeled (see *Advice*, item 2). The individual storage location of each sample is recorded in the sample tracking database. These samples are stored in the vapour phase of liquid nitrogen (LN) in a secure storage area.

Freezer and LN facilities are monitored; maximum and minimum temperatures are recorded in real time. Freezers and cryovessels are linked to a data logged, continuous temperature monitoring system using internal temperature probes. This feeds into a wireless callout system which follows a callout rota to key staff. Temperature excursions outside the set ranges trigger both audible alarms and the wireless callout system. The liquid nitrogen facility contains oxygen depletion monitors and an automatic cryofilling system.

Emergency contingency freezers and a LN cryovessel are available in the same storage area in the event of storage failure.

Human tissue samples are mainly used to depletion and disposed of according to health and

safety and HTA guidelines. Human tissue that is unused is disposed of within two years of receipt, after consultation with the supplier. The date and person responsible for disposal are recorded on the sample tracker database (see *Advice*, item 2).

The timetable for the site inspection was developed after consideration of the establishment's previous inspection report, compliance update information and communications with the HTA since the last inspection. The inspection included a visual inspection of the site (research laboratory and storage facilities). Meetings were held with the DI (President, Chief Scientific Officer and Services Manager), the PD (Quality Specialist), the Team Leader (Cellular Services) and the Director of Sales. A documentation review and audits of traceability were also carried out.

Traceability audits were performed on fifteen samples, from four different suppliers, which were tracked from the sample database to LN storage locations. Three samples, from three individual suppliers, were tracked from the sample database to LN storage locations. The MTAs of these samples were checked for confirmation of donor consent. Full traceability was found.

Inspection findings

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

Compliance with HTA standards

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.	GQ6(a)	There is a comprehensive suite of risk assessments (RAs) covering HTA-licensed activities (RA11_V1.2; *Management of Human Tissue Samples*). The documents listed under 'Mitigations' for each RA is stated in the text. The DI is advised to list these documents also in the *Risk Matrix, Appendix 1* to allow for easy reference.
2.	T1(a)	Samples obtained from suppliers, which are identical and are derived from pooled donations, are identified by the original lot number and not relabelled, resulting in several vials having the same identifier. In the event of expansion of activities with an increase in sample numbers, the DI is advised to consider relabelling these samples with unique identifiers to mitigate any risk of loss of sample traceability.
3.	T2(b)	Most samples are used to depletion. The remainder of samples are disposed of on expiry, after two years from receipt. The date and the person responsible for the disposal of samples are recorded in the sample tracking database. The DI is advised to include the reason for disposal to ensure that a record is kept of any samples that have been disposed of due to withdrawal of consent. The DI is advised to update the SOP CA0088V3.3 *Sample Handling and Close Out Procedures for Customer Studies* to include this.

Concluding comments

During the site visit inspection of the establishment, several areas of strength were noted:

- There is a comprehensive induction training schedule for all staff which includes the management of human tissue samples, the HTA and the associated regulatory requirements. Staff are required to pass an assessment on this topic and to include training certificates as evidence in their training folder.
- There is a robust and comprehensive quality management system. The establishment is ISO 9001 certified and as part of this, an external audit of current documentation has been carried out and a formal gap analysis against the new HTA standards performed. Any areas of non compliance against the new HTA standards have been rectified.
- The staff working under the licence are part of a small team and appear to work well

together.

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

Report sent to DI for factual accuracy: 19/10/2107

Report returned from DI: 1/11/17

Final report issued: 6/11/17

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice. b) Consent forms are available to those using or releasing relevant material for a scheduled purpose. c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice. d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice. b) Records demonstrate up-to-date staff training. c) Competency is assessed and maintained.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities. b) There is a document control system. c) There are change control mechanisms for the implementation of new operational procedures. d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff. e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities. b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training.
b) There are documented induction training programmes for new staff.
d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.
b) Risk assessments are reviewed regularly.
c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.
c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity.
c) Storage conditions are monitored, recorded and acted on when required.
d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
c) Staff are provided with suitable personal protective equipment.

Appendix 2: Classification of the level of shortfall

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions

   or

   A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

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

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall that:

   - poses a risk to human safety and/or dignity, or
   - indicates a failure to carry out satisfactory procedures, or
   - indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines, or
   - has the potential to become a critical shortfall unless addressed

   or

   A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

   In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards.

This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based or site visit.

In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.