



Site visit inspection report on compliance with HTA licensing standards

Adaptimmune Ltd

HTA licensing number 12635

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**

22 November 2018

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.

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

The HTA has given the DI advice with regards to some aspects of consent training, document control, auditing, risk assessments and equipment monitoring.

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 licensed activities carried out at Adaptimmune Ltd (the establishment). The establishment is licensed for the storage of relevant material that has come from a human body for use for a scheduled purpose, under the Human Tissue Act 2004 (HT Act). Human samples are stored for use for the scheduled purpose of 'research in connection with disorders, or functioning, of the human body'. The establishment has been licensed since December 2015 and this was the first routine site-visit inspection to assess whether it meets the HTA's standards.

The establishment is an early clinical stage biotechnology company within the field of immunotherapy. Relevant material is obtained from clinical trials, internal volunteers, third party providers or purchased from commercial suppliers. Most samples are blood but also include tissue and bone marrow.

Fresh blood samples are obtained in-house. The Personal Investigator (PI) is responsible for the studies and fills out a blood request form each time samples are required. Applications are reviewed by 'Consent Experts' to ensure that the consenting process in place covers what is required. Fully trained phlebotomists are responsible for contacting donors, arranging appointments and obtaining consent (see *Advice*, item 1). Consent is sought using a consent form and an accompanying information sheet that reflect the requirements of the HT Act and HTA's Codes of Practice. After consent is sought, samples are obtained, de-identified and coded before being transferred into the laboratory.

For clinical trial samples and commercially sourced material, consent is obtained by the external centres and there are agreements in place to ensure that consent is obtained in accordance with the requirements and covers the studies that are being conducted by the establishment. Although some samples sent are imported from outside the UK and therefore the consent provisions of the HT Act do not apply the establishment ensures that valid consent has been obtained in accordance with the HTA's good practice guidance. Samples are sent to the establishment using tracked couriers and there are robust procedures in place to ensure that samples and their chain of custody are tracked from arrival to storage to disposal or use. Although individual departments use slightly different systems for tracking, the establishment are currently working towards a standardised procedure and implementing an electronic sample management system that will be rolled out site wide (see *Advice*, item 5).

The establishment is located within a science park. Access to the building and to the laboratories is restricted to authorised personnel only. Visitors must be accompanied and are required to sign in and out at the entrance. Samples are stored throughout numerous laboratories. Samples are stored in fridges, freezers, liquid nitrogen tanks or in cabinets at room temperature. All temperature controlled facilities are fitted with automated alarms that

are triggered by deviations from the set acceptable temperature ranges. If temperatures go out of range, an external monitoring service alerts relevant members of staff by text and email, 24 hours a day (see *Advice*, item 6). Facilities are well maintained and the liquid nitrogen storage tanks are subject to annual servicing, although the fridges and freezers are not (see *Advice*, item 7). There are contingency arrangements in place for all storage facilities.

Description of inspection activities undertaken

The inspection timetable was developed in consideration of the activities conducted under the licence, compliance update information, discussions with the DI and previous communications with the HTA. The inspection included a review of the establishment's procedures for conducting activities under the licence and interviews with staff involved in consent seeking, quality management and sample management. The inspection also included a visual inspection of the areas where samples are stored under the licence and audits of sample traceability. Audits of the following, randomly-selected samples were conducted, covering all storage conditions:

- Three samples from storage to record of consent.
- Five samples from record of consent to storage.
- Two disposal records.

All samples were fully traceable.

Inspection findings

Compliance with HTA standards

All standards were fully met.

Advice

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

No.	Standard	Advice
1.	C2(b)	The DI is advised to record dates for when staff refresher training is due. This will ensure that refresher training is flagged-up and staff knowledge and competency is kept up-to-date.
2.	GQ1(b)	Although the document control system records all relevant information – for example, version number, author, review date - the DI is advised to include this information on the front pages of SOPs to assist the reader in identifying the most recent and up to date documents.

3.	GQ2(a)	<p>The establishment's audit schedule does not include procedural audits. The DI may wish to add these to the schedule. Horizontal audits by staff involved in the processes will ensure that SOPs accurately reflect the practices and will identify areas for improvement as well as training needs.</p> <p>Further guidance on audits can be found in the HTA's research sector licensing standards and guidance document, which is available on the HTA's website.</p>
4.	GQ6(a)	<p>Although risk assessments detail how to mitigate risk, the DI is advised to reference the relevant SOPs within the assessments. For the majority of risks relating to licensable activities, following the correct procedure will reduce risks and by including this information it will provide a useful resource for staff.</p>
5.	T1(a)	<p>With the establishment continually expanding the DI is encouraged to continue implementing the LIMS system resulting in a more streamlined approach to sample management across departments.</p>
6.	PFE2(c)	<p>Freezer alarms are often triggered by staff during day to day use however the DI is advised to implement formal tests of storage temperature alarms. This will help to ensure that the alarms are functioning as expected.</p> <p>The DI is advised to ensure that temperature records are monitored for trends. This may help staff to identify when storage conditions may be deteriorating and might alert staff to impending equipment failure.</p>
7.	PFE3(a)	<p>Although maintained, with contingencies in place, the fridges and freezers do not undergo routine servicing. The DI is advised to consider whether some pieces of equipment should be placed under regular maintenance contracts in order to mitigate the risk of failure.</p>
8.	N/A	<p>The DI is advised to make staff aware of the HTA's bi-monthly newsletter, which may help them to keep abreast of relevant information for the areas they work in.</p>

Concluding comments

This report outlines the first routine inspection of the establishment.

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.

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

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

Report sent to DI for factual accuracy: 10 December 2018

Report returned from DI: 12 December 2018

Final report issued: 12 December 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.

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
<p>a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.</p> <p>b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.</p> <p>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.</p> <p>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.</p> <p>e) Language translations are available when appropriate.</p> <p>f) Information is available in formats appropriate to the situation.</p>
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
<p>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.</p> <p>b) Records demonstrate up-to-date staff training.</p> <p>c) Competency is assessed and maintained.</p>
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
<p>a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.</p> <p>b) There is a document control system.</p> <p>c) There are change control mechanisms for the implementation of new operational procedures.</p> <p>d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.</p> <p>e) There is a system for managing complaints.</p>
GQ2 There is a documented system of audit
<p>a) There is a documented schedule of audits covering licensable activities.</p> <p>b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.</p>

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.
- c) Training provisions include those for visiting 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.
- b) Where relevant, storage arrangements ensure the dignity of the deceased.
- 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.