Inspection report on compliance with HTA licensing standards
Inspection date: **27 September 2022**

ADC Therapeutics UK Limited

HTA licensing number 12664

Licensed under the Human Tissue Act 2004

Licensed activities

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose	Removal from the body of a deceased person (otherwise than in the course of an anatomical examination or post-mortem examination) of relevant material of which the body consists or which it contains, for use for a scheduled purpose other than transplantation
ADC Therapeutics UK Limited	Licensed	Not licensed

Summary of inspection findings

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

ADC Therapeutics UK Limited ('the establishment') was found to have the met most of HTA's standards; however, two minor shortfalls were identified against one standard for Governance and quality systems (Standard Operating Procedures (SOPs and risk assessments).

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 assessment.

Compliance with HTA standards

Standard	Inspection findings	Shortfall
GQ1 All aspects of the establishment's work are governed by documented policies and procedures as part of the overall governance process		
GQ1(a) Ratified, documented and up-to-date policies and procedures are in place covering all licensable activities	The overarching document ACDT-RES-001 lacked procedural details and the full range of procedures that are relevant to licensed activities, are not documented.	**Minor**

GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored		
GQ6(a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Code of Practice	The establishment's risk assessment did not cover the range of risks for all relevant practices and processes.	**Minor**

Advice

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

Number	Standard	Advice
1.	GQ1(a)	The establishment purchases tissue slides from an external provider. The tissue slides have a one-year shelf life for storage which means that after this period they may not be useful for research use. Based on discussions with the PD, it is likely that the slides would be disposed of after one year. The DI may wish to consider documenting (for example, in the existing disposal policy) that tissue slides may be disposed of after a one- year period.
2.	GQ1(a)	The establishment's licensed activities rely on a limited number of experienced staff; however, the SOP governing HTA activities - ADCT-RES-001 - does not provide comprehensive procedural details, set out in a stepwise fashion. The DI is advised that SOPs should be understandable to enable new staff to follow a procedure from beginning to end. They should be detailed enough to ensure uniformity between staff in the performance of a specific function and should be followed to the letter by all staff who have been appropriately trained.
3.	GQ1(d)	Although there are meetings where HTA activities are discussed, these are not formally documented. The DI is advised to consider minuting these meetings, to record what was discussed as well as any actions agreed.
4.	GQ2a)	The establishment has undertaken audits on a six-monthly basis. One of the audits focusses on traceability and the other focusses on compliance with the HTA's standards. The audit against the HTA's standards lacked detail on what evidence was reviewed to assess compliance with a specific standard. The DI is advised to record greater detail on the audit proforma for the audit against the HTA's standards so that it is clear what evidence was reviewed to provide assurances and whether it demonstrated compliance.

5.	GQ4(a)	The establishment's current system for managing traceability does not record the position of the slides accurately and this issue has been actively managed by the establishment. The establishment will be moving over to a new system to manage traceability in due course and any errors in positions will be corrected in the new traceability system. After the new system is implemented, the DI is advised to consider carrying out an audit to provide assurances that all the sample positions have been transcribed correctly.
6.	GQ6(a)	Procedural steps on the receipt of slides were included as part of the risk assessment. In addressing the shortfall against GQ1(a), the DI is advised to ensure that procedural information is recorded in procedural documents, such as SOPs.
7.	PFE2(c)	To strengthen the awareness and management of appropriate storage conditions, the DI is advised to consider adding signs that define minimum and maximum fridge alarm temperatures.
8.	PFE2(d)	The DI is advised to review contingency plans (currently documented in ADCT-RES-001), making appropriate revisions to ensure that the text provides clear instructions to staff on how to manage a failure in storage conditions and to which designated fridge the slides can be moved

Background

The establishment is biotechnology company involved in research to develop treatments for cancer. The establishment used to store Peripheral Blood Stem Cells (PBMCs) but currently purchases and stores only human tissue slides. This was the third HTA inspection of the establishment, with the previous two inspections taking place in 2014 and 2019.

Description of inspection activities undertaken

The HTA's regulatory requirements are set out in Appendix 1. The Regulation Manager covered the following areas during the inspection:

Standards assessed against during inspection

Of the 47 HTA standards, 38 were assessed (standards published 3 April 2017). Standards C1(a)(b),(d),(e),(f) and C2(a),(b),(c) and T1(f) were not applicable at the time of the inspection.

Review of governance documentation

A number of documents were reviewed during the assessment, which included but were not limited to: SOPs for licensable activities, key policies, traceability audits, staff competency records and records relating to traceability.

Visual inspection

There was no site visit; however, the establishment provided a virtual tour of the licensed storage area. This was followed up by a meeting with relevant staff members to discuss the PFE standards.

Audit of records

No traceability audits were carried out; however, a review of the establishment's traceability audits was undertaken as part of the assessment. The Regulation Manager had no concerns with the audits presented during the assessment.

Meetings with establishment staff

A roundtable discussion was carried out with establishment staff, which included the CLHc (Corporate Licence Holder contact), DI and PD (Person Designated).

Report sent to DI for factual accuracy: 21 October 2022

Report returned from DI: 4 November 2022 (no comments)

Final report issued: 8 November 2022

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 26 May 2023

Appendix 1: The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the DI 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 DI 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 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.

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 Human Tissue Act 2004 (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 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:

   - A notice of proposal being issued to revoke the licence
   - Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.
   - A notice of suspension of licensable activities
   - Additional conditions being proposed
   - Directions being issued requiring specific action to be taken straightaway

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 Codes of Practice, 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 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 the final inspection report. Establishments 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 inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next routine inspection.

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