

# Research sector review: July 2016



A summary of HTA inspection findings, advice and learning



# Executive Summary

In March 2015, the HTA completed the first round of inspections for all the establishments we have licensed in our research sector since the HTA's inception. This review presents the trends found on those inspections, as highlighted through our reported findings. Through the review, we also aim to share good practice and promote improvements. Through our regulation, we want to encourage and support a culture of responsible custodianship, something we believe is already present in the research sector. In fostering this environment, the drive for improvement and high standards is shared with the people best placed to effect long-lasting changes and deliver continuous improvements at local, national and international levels.

We hope that this report will be useful to people working in the sector as well as to members of the public who have an interest in human tissue research. Our website remains the most up-to-date source of information for all the sectors we regulate and includes not only codes of practice and other documents but also guidance produced in collaboration with other bodies working within the research regulatory environment.

In the period November 2010 to March 2015, we conducted 87 site visit inspections for the remaining uninspected establishments licensed within our research sector. During these inspections, we identified a total of 103 shortfalls against the HTA's licensing standards and offered 517 items of advice. In more than half of the inspections, no shortfalls were identified. This summary report shows that HTA-licensed research establishments generally met the HTA's licensing standards. We found that the main areas which required improvement were related to governance and quality systems. This review summarises our key learning points for improving practices in these areas, as well as in other areas where shortfalls were identified.

High levels of compliance and good practices were observed throughout our inspections, which confirm the HTA's long-held view of the research sector and supports its 'low risk' reputation.



# Introduction

1. The Human Tissue Authority regulates the removal, storage, and use of human bodies, body parts, organs and tissue for activities such as research, patient treatment, post-mortem examination, anatomical examination, and public display. We license establishments that carry out these activities in England, Wales and Northern Ireland, and inspect them to make sure regulatory requirements are met. We also give approval for organ and bone marrow donations from living people.

2. 'Research in connection with disorders, or the functioning, of the human body' is a scheduled purpose under the Human Tissue Act 2004 (the HT Act). At the time of final drafting, we licensed 154 establishments in our research sector. Due to the number of associated satellite sites, the total number of licensed sites in our research sector is 289, making it the second largest sector we regulate in terms of licensed sites. This figure grows each year but gives only a limited picture of human tissue research activities, which are widely spread throughout the establishments licensed in our other sectors. Due to the proportionate approach in which we license, establishments licensed in our other sectors are permitted to store human material for research and a substantial proportion of these do that. In addition to storing material for research, many establishments are also involved in storing human tissue for other scheduled purposes; for example, clinical audit, quality assurance and performance assessment.

3. In March 2015, the HTA completed its first cycle of site visit inspections for all the establishments we have licensed in our research sector since our inception. This report contains a summary of the inspection findings and main trends in compliance with the HTA licensing standards. The aim of the report is to promote shared learning within the sector, with a particular focus on areas requiring further improvement, as well as highlighting good practices.

4. We conduct site visit inspection of licensed establishments to assess their compliance with our licensing standards and to offer advice on how they can improve. As the research sector has been considered to be of low regulatory risk, inspections of research establishments have been scheduled across longer periods of time than in other sectors.



5. Site visit inspections comprise a visual inspection of the premises and facilities, meetings with staff and a review of policies and procedures. Establishments are assessed against a set of licensing standards, grouped into four main categories: consent (C); governance and quality systems (GQ); premises, facilities and equipment (PFE), and; disposal (D).
6. The findings from site visit inspections are presented in inspection reports. Since November 2010, we have produced exception-based inspection reports, where only those HTA standards that have not been met are detailed. Inspection reports also include advice and good practice.
7. To be transparent about the regulatory action we have taken, and to provide opportunities for learning across the sector, all inspection reports since November 2010 have been published on our website.
8. Where a HTA licensing standard has not been met, a shortfall is identified and classified as 'critical', 'major' or 'minor'. We work with establishments to address shortfalls through corrective and preventative action (CAPA) plans. The timeframe for completion of CAPAs depends on the classification of the shortfall. Critical shortfalls are the most serious and are expected to be addressed immediately. Major shortfalls require CAPAs to be completed within one to two months of the final report being issued. Minor shortfalls are expected to be addressed within three to four months of the final report being issued. Further information about our inspection processes can be found in Appendix 1.
9. Where a HTA standard is fully met but we identify an area of practice that could be further improved, we provide advice to the establishment and include this in the inspection report. Our inspection reports also highlight areas of good practice identified during inspections. By publishing examples of good practice in our inspection reports and in summary publications, we aim to share people's successes and provide support to others.

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# Overview of the research sector and inspection findings

9. This report includes an analysis of the shortfalls, advice, and good practice identified during the 87 site visit inspections undertaken from November 2010 to March 2015. Inspections conducted prior to November 2010 have been excluded from this review because the reporting of inspection findings changed after this time. Previous summary reports for this sector provide an overview of our inspection findings prior to the change. A list of the establishments inspected in this period and summarised in this report is provided in Appendix 2.

10. At the time of final drafting of this report, there were 289 establishments licensed in the research sector. These comprise 103 standalone premises and 51 hub sites associated with a total of 135 satellite sites.



289 establishments licensed in the research sector

## Inspection findings - shortfalls

11. No critical shortfalls were identified during the 87 inspections and, in 48 inspections (55%), no shortfalls were found.

12. Five major shortfalls were found during four of the 87 inspections, and these were against HTA standards C1, C2, GQ6 and GQ8. A total of 103 minor shortfalls were found during 37 inspections and these were identified across all of the HTA standards, except GQ3 (staff training) where no shortfalls were found. One minor shortfall was not against a particular standard and was due to the lack of Person Designated (PD) at a satellite premises.

13. The highest numbers of minor shortfalls were identified against standards, GQ1, GQ2 and GQ8. The main weaknesses were a lack of documented procedures or detail covering licensable activities, an absence of regular governance meetings and a lack of risk assessments. A total of 20 minor shortfalls were found against standard GQ8 (risk assessments), the highest number against any single standard.

14. Figures 1 and 2 show the distribution of minor and major shortfalls across the HTA standards.

### Minor shortfalls

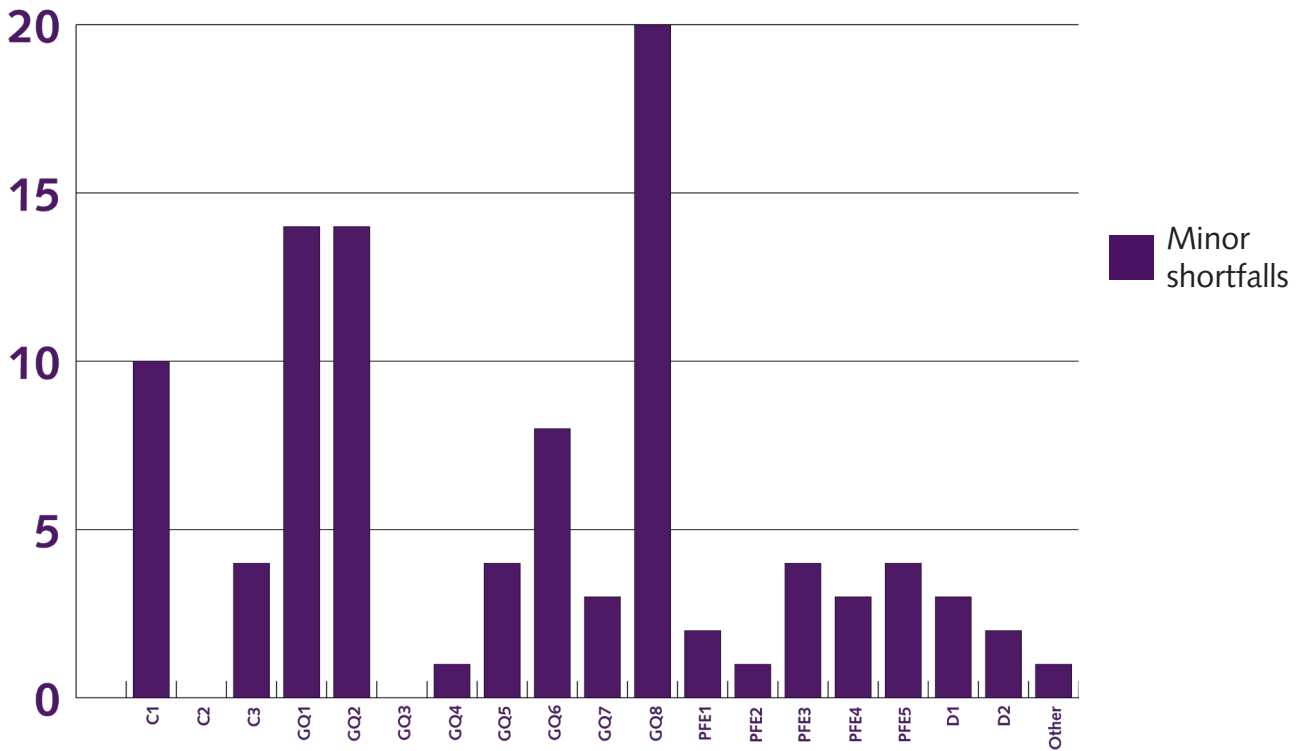


Figure 1: Distribution of minor shortfalls identified across HTA licensing standards (inspections undertaken November 2010 – March 2015)

### Major shortfalls

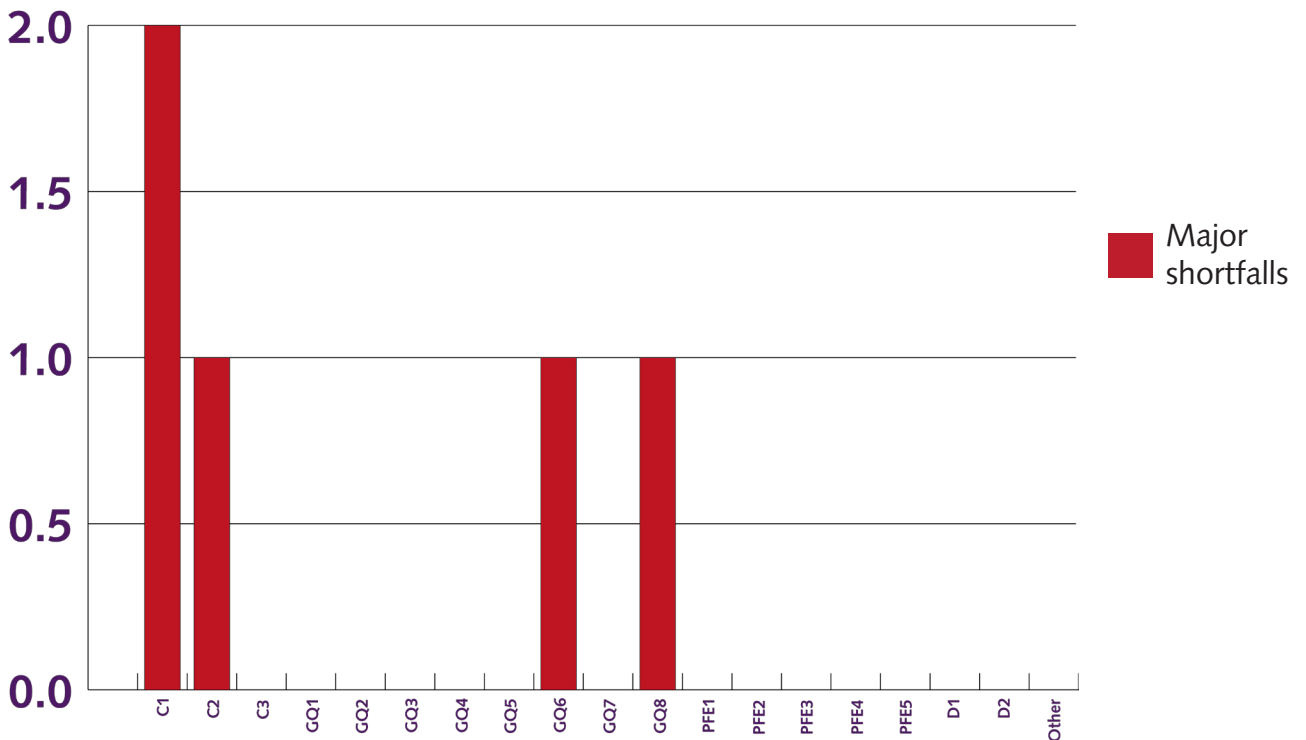


Figure 2: Distribution of major shortfalls identified across HTA licensing standards (inspections undertaken November 2010 – March 2015)

# Advice

15. A total of 517 items of advice were given during 87 inspections, which emphasises the importance we place on our role in providing advice. The most number of advice items were against our governance and quality systems standards, particularly standards GQ1 (81 items of advice were given), GQ2 (49 items) and GQ8 (53 items). There were 56 advice items against standard PFE3 and 41 items against standard C1.

16. Fourteen items of advice were not specifically against a particular standard. Most of these advice items had a focus on adding Persons Designated (PDs) to licensing arrangements, strengthening the governance of licensed activities.

17. Figure 3 shows the distribution of advice provided across the HTA standards.

## Advice

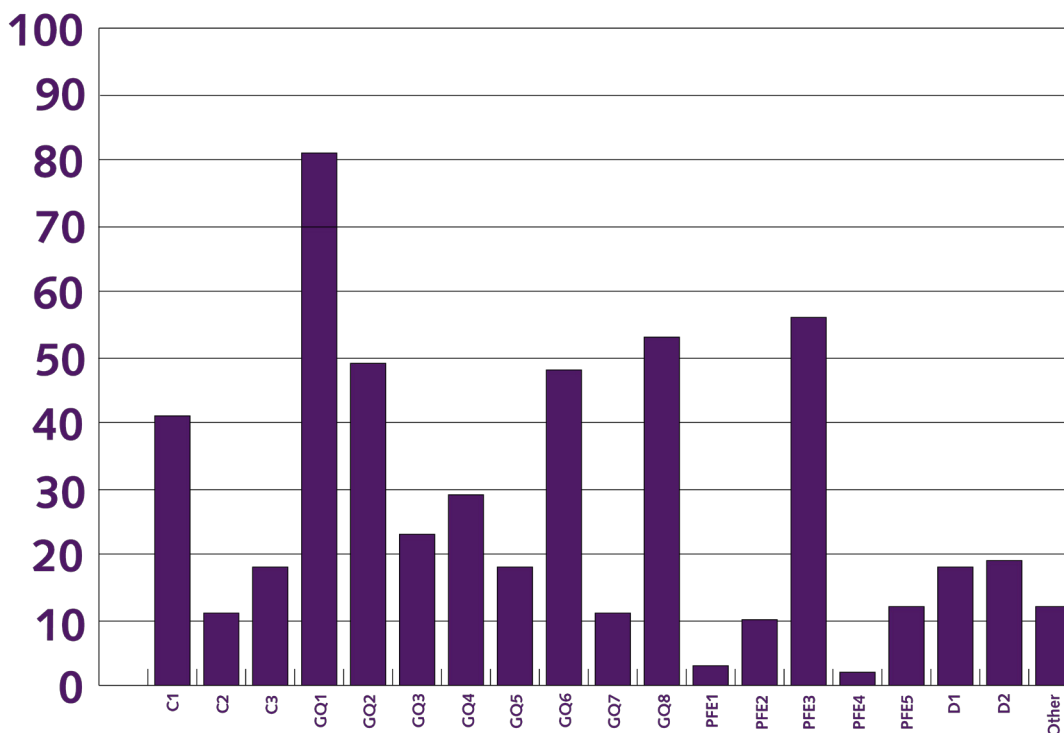


Figure 3: Distribution of advice given to establishments across HTA licensing standards (inspections undertaken November 2010 – March 2015)

## Compliance with HTA standards

20. Overall, establishments in the research sector were found to be compliant with the HTA's licensing standards, with no shortfalls being identified in more than half of inspections. The following sections highlight the key areas against our standards which were identified as requiring further improvement. Advice and learning points are also included, along with the good practice noted during inspections.

## Consent standards (C1-C3)

### Key findings

21. Consent is the fundamental principle of the HT Act. Inadequate SOPs covering the consent process, as well as concerns about consent forms and patient information sheets, were all issues identified during inspections. We also identified that staff training resources on consent were sometimes limited and required further improvement.

### *C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 and as set out in the code of practice*

22. Two major shortfalls were found against the standard C1.

23. In one case, our audit findings showed there was a lack of assurance that the consent process had been followed in accordance with local procedures. There was ambiguity surrounding the physical completion of consent forms, which made it unclear whether a participant had provided their consent for research. Following the site visit inspection, and working with the HTA, an investigation was undertaken by the establishment and the small number of samples associated with ambiguous consent were disposed of and consent was re-sought from with the donors. A number of remedial actions were taken by the establishment to prevent any similar issues arising in the future.

24. In a separate case, researchers had an inconsistent approach to seeking consent due to the absence of a documented consent procedure. Establishments that have multiple research groups working under the governance of a HTA licence should follow consistent procedures to eliminate the risk of obtaining invalid consent. A documented procedure can be used to reinforce to staff seeking consent which aspects must be discussed with the donor for consent to be informed and valid.



25. The HT Act 2004 does not specify the format in which consent is given or documented. However, it is usual practice for consent forms to be completed by donors for research purposes. There may be occasions where oral consent may be sought and, where this is the case, the person who obtains the consent should document it in the participant's file or medical case notes. On one inspection, it was found that there was a reliance on staff to provide the assurance that consent was in place, which often but not consistently, was backed up with a consent form. A robust consent process reduces the risk of human tissue being stored without consent.

26. The consent requirements of the HT Act 2004 do not apply to imported material. However, as good practice, licensed establishments importing human tissue from outside England, Wales and Northern Ireland should have in place, agreements that describe the consent arrangements for material that is supplied for research use. This is particularly important when individual consent forms are not provided to licensed establishments. A minor shortfall was identified at a licensed establishment that was importing human tissue without having an agreement in place to confirm that only material which had consent for storage and use for research was supplied.

27. A licensed establishment was given a minor shortfall against standard C1 because agreements with a third party tissue provider did not refer to the legal requirements for consent under the HT Act 2004 for human tissue to be stored after the completion of the clinical trial or the expiry of NHS Research Ethics Committee (NHS REC) approval.

**“A robust consent process reduces the risk of human tissue being stored without consent.”**



# Advice and learning: C1

28. Forty-one items of advice were provided against standard C1.

29. Establishments should keep their approaches to completing consent forms under review. Variations in the approaches taken to completing consent forms were seen during inspections. This was because documented procedures did not contain comprehensive information about how consent should be recorded. The format in which donors are expected to complete consent forms should be described in procedures; for example, a donor may be required to tick or provide their initials against specific consent provisions to confirm their consent.

30. Consent forms and information sheets should contain comprehensive information to enable donors to make an informed decision about participating in research. Donors should be provided with information about; the types of samples to be donated; the frequency of donation and all anticipated research uses (including genetic research). Where samples are being prospectively collected for research involving DNA analysis, it should be made clear to the donor that their bodily material will be used for this purpose.

31. Researchers may purchase human tissue from tissue providers in order to conduct research. It is unusual to receive individual consent records in these instances. The HTA provided advice to establishments to formalise their supply arrangements to assure themselves that they receive human tissue for which the associated consent sufficiently covers the work they are undertaking. With this in mind, establishments may wish to review the template consent forms relied on by tissue suppliers.

## C2 Information about the consent process is provided and in a variety of formats

32. One major shortfall was found against standard C2 at an establishment. This was due to a combination of several minor shortfalls relating to deficiencies in the consent process and the information provided to donors. Information for donors, including the exclusion criteria, was not routinely being given in advance of consent being sought. Additionally, as this procedure had not been formalised or documented, an inconsistent approach amongst staff seeking consent, posed a risk that donors may not be suitably excluded from the research.

33. A weakness in the traceability system was also identified at this establishment. Research staff could contact fellow staff members to provide repeat donations. Although a coding system had been adopted, research staff were able to break the code and approach specific members of staff to donate again. This information was not explained to donors during the consent process and they were unaware that they may be approached again.

## Advice and learning: C2



34. Eleven items of advice were provided against standard C2.

35. If required, information sheets should be available in different languages and formats. It was sometimes found that the written information provided to donors required improvement as it lacked the detail to enable donors to fully understand the research.

36. Information sheets should also set out where, and for how long, human tissue will be stored for all envisaged uses.

37. Establishments should consider their approaches to seeking consent and consider whether consent for future uses of human tissue samples in other studies is needed, as well as permission from the participant to be re-contacted for further donations or consent.

## *C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent*

38. Four minor shortfalls were found against standard C3.

39. Tissue from the deceased (for example, obtained during a post-mortem examination) may be used for research with the consent from a person ranked highest in the hierarchy of qualifying relationships set out in the HT Act (see HTA's code of practice on post-mortem examination) This consent will be usually sought at the same time as consent for the post-mortem examination is being sought. A minor shortfall was given to one establishment using deceased tissue in research because there was no system in place to ensure that all clinicians seeking consent were appropriately trained.

40. The other shortfalls identified against standard C3 were primarily due to establishments being unable to demonstrate the availability of suitable consent training resources, in order to ensure staff training is kept up to date. Furthermore, DIs were advised to maintain a log of staff who had attended consent training.

## Advice and learning: C3



41. Seventeen items of advice were given against standard C3.

42. Consent training should be available to all staff involved in seeking consent for research. It is important that consent training is not considered a one-off event and that proficiency in seeking consent is upheld. There is no set requirement for the frequency of consent training. Regular consent training should aim to ensure that staff involved in seeking consent are kept informed about the requirements of the HT Act 2004 and of any relevant good practice.

43. Clinical staff may be involved in seeking consent within their professional capacity, which is usually part of patient treatment. However, there are differences in consent for patient treatment and consent for research. Consent to treatment and examination is covered by the common law and Mental Capacity Act 2005. Under the HT Act, consent must be in place for the storage and use of tissue from the living and for the removal, storage and use of tissue from the deceased.

44. Establishments should ensure that:

- the training covers the consent requirements of the HT Act;
- a log of staff attending consent training is maintained;
- refresher consent training is available to staff involved in seeking consent;
- the consent process is subject to review through process audits to ensure it is robust;
- training is updated when legislation has changed or when new policies or practices have been implemented.

## Good practice: C1-C3



45. Overall, establishments demonstrated good practice in relation to the consent standards.

46. Some establishments had given particular consideration to the development of age-appropriate information sheets to ensure that donors of all ages were able to provide informed consent for their tissue to be stored and used for research.

48. Although the consent requirements of the HT Act do not apply to imported material, establishments had put in place agreements with tissue providers to confirm their consent arrangements aligned with good practice principles.

47. Consent training was also often delivered to a high standard. It was delivered either as part of internal HTA training or Good Clinical Practice (GCP) training, which is mandatory for staff working in clinical trials.

49. Establishments had carefully considered consent training requirements, with DIs often taking responsibility to train staff on a regular basis, especially new members of staff. Refresher training was also often made available to staff involved in seeking consent.

# Governance and Quality systems standards (GQ1-GQ8)

## Key findings

50. Despite staff demonstrating a clear understanding of local procedures, these were not always formalised in documented procedures. Audits sometimes required strengthening to ensure that arising actions were followed up. In terms of advice, standard GQ1 (documented policies and procedures) received the highest number of items. Most shortfalls were identified against standard GQ8 (risk assessments).

*GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process*

51. Fourteen minor shortfalls were identified against standard GQ1.

52. Although staff could often demonstrate an understanding of procedures, at times, these had not been formalised as documented procedures. Furthermore, some establishments with different research groups did not have overarching SOPs in place. Research groups storing and using human tissue under the governance of a HTA licence were frequently relying on their own group's procedures. Consequently, staff demonstrated an inconsistent approach in carrying out licensable activities, leading to variability in practices and risks that secure governance arrangements could break down.

53. Governance meetings provide excellent opportunities for staff involved in licensed activities to discuss relevant issues or concerns, and to share learning. Minor shortfalls were found because some establishments did not have meetings where relevant issues could be discussed.

**"Governance meetings provide excellent opportunities to discuss relevant issues or concerns, and to share learning."**



# Advice and learning: GQ1

54. Eighty one items of advice were given in relation to standard GQ1. This standard received the highest number of advice items compared to the other standards.

55. Importantly, establishments must ensure that SOPs contain accurate information, reflecting current practices. It was found during inspections, that documents had not always been updated following a change in a procedure, posing a risk that staff may inadvertently follow out-dated practices.

56. The value of governance meetings is reinforced above (refer to paragraph 53). Notes (or minutes) of meetings should be made to record what was discussed and enable agreed actions to be captured, as well as to provide an opportunity for any changes to be communicated to staff undertaking licensed activities.

57. All documents should be subject to version control and managed to maintain a revision history of all changes. As good practice, documents should also be reviewed regularly, whether or not a change in procedure is required. This acts as a confirmation that procedures have been reviewed. Documents should also contain the following:

- 'effective from' date;
- review date;
- pagination;
- author and reviewer names.

## *GQ2 There is a documented system of quality management and audit*

58. Fourteen minor shortfalls were identified against standard GQ2.

59. Audits allow establishments to review their compliance with their own procedures and HTA standards. The majority of shortfalls identified against standard GQ2 were due to the absence of a documented audit schedule encompassing licensed activities, together with an inconsistent approach to following up actions arising from the audits.

60. CAPA plans are frequently used by establishments to document and address shortfalls identified during audits. Commonly, a CAPA plan will identify a staff member allocated to resolve a particular issue. Formal closure of a CAPA plan action should describe the action taken. Establishments sometimes did not have formal procedures to deal with actions arising from audits. Thorough follow-up of agreed actions and their closure, is important for the full audit process to be successful.

61. A minor shortfall was found at one establishment where discrepancies during tissue sample traceability audits were identified. Although a wide range of audits were being carried out, tissue traceability audits had not been carried out to a regular schedule across all tissue collections. Internal traceability audits act as useful assurances to establishments that their tissue tracking systems and procedures are robust.

62. Establishments use a variety of different quality management systems to ensure that the review and approval of all documents is subject to document control. Shortfalls were identified where establishments lacked procedures detailing the format, use and control of SOPs as part of the overall quality management system.

**“Internal traceability audits act as useful assurances to establishments that their tissue tracking systems and procedures are robust.”**





# Advice and learning: GQ2

63. Forty nine items of advice were provided against standard GQ2.

64. The largest proportion of advice items was linked to the audit approaches taken by establishments. In most cases, even though establishments had audit schedules, and were carrying out suitable audits, advice was given in relation to how audit findings, or any actions arising, should be documented and closed.

66. Establishments may use vertical and horizontal audits to assure themselves that human tissue samples and records are fully traceable from consent to disposal and that SOPs accurately reflect current practice. Establishments can also use process or observational audits to assess whether or not procedures take place in accordance with documented procedures.

65. To strengthen the audit process, establishments with PDs in several research groups were advised to audit one another's research areas to help promote shared learning, improve consistency across groups and to provide an independent audit perspective.

67. A robust quality management system (QMS) enables staff carrying out licensed activities to have access to the most current procedures and be notified of changes. Although all establishments had a QMS in place, this was not always being used effectively, leading to inadequate control of documents as well as inconsistent approaches to reviewing documents.

*GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills*

68. No shortfalls were found against standard GQ3.

## Advice and learning: GQ3



69. Despite no shortfalls being identified against standard GQ3, 23 items of advice were provided to establishments to raise staff awareness about the types of training resources available to them and to ensure that staff have access to training during inductions, as well as to refresher training.

70. Staff are expected to have regular appraisals and personal development plans in place to highlight continuous professional development.

### *GQ4 There is a systematic and planned approach to the management of records*

71. One minor shortfall was identified against standard GQ4. Compounding this weakness, it was found that the establishment did not have a regular audit of record content to check for completeness, legibility or accuracy in place and neither was there a planned schedule of audits that encompassed all areas and aspects of licensable activities.

## Advice and learning: GQ4



72. Twenty nine items of advice were given against standard GQ4.

73. Records may be subject to amendments. Some establishments routinely used correction fluid to correct any errors that were made. They were advised to correct errors by placing a single line through the error, as well as placing their initial and date against the amendment. By maintaining records in this manner, they are more readily auditable. Records should be written using ink, as amendments using pencil lead can be modified or erased easily. One establishment routinely using pencils to complete forms was advised to change this practice, as it would not ensure an indelible record.

74. All consent forms, tissue traceability records and associated forms should be stored securely and, if electronically stored, must be adequately backed-up.

75. Establishments are expected to assure themselves that electronic systems ensure data protection (Data Protection Act 1998), confidentiality and public disclosure ('whistle-blowing').

## *GQ5 There are documented procedures for distribution of body parts, tissues or cells*

76. Four minor shortfalls were found against standard GQ5.

77. Some establishments involved in transferring human tissue were unable to provide evidence of agreements with their tissue suppliers.

78. Documents seen during inspections sometimes lacked sufficient information about distribution procedures. In addition, establishments did not have formalised, documented procedures in place providing information about how tissue would be accessed or removed from the premises.

## Advice and learning: GQ5



79. Seventeen advice items were given against standard GQ5.

80. Documented agreements need to contain sufficient information about the preservation, storage, given consent and disposal of human tissue. The responsibility to ensure tissue traceability during storage, use and disposal should also be made clear.

81. Some establishments use a form to document information about the tissue to be distributed before a formal agreement is drawn up. Recording information in this way enables the receiving establishment to make an assessment of the supplying establishment's compliance with the HT Act 2004 before formalising arrangements and accepting tissue samples. This good practice was shared with establishments as advice during the inspections carried out in the period covered by this report.

## *GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail*

82. Eight minor shortfalls and one major shortfall were identified against standard GQ6.

83. Sample traceability is a key component of our regulatory framework. The majority of minor shortfalls were due to inadequate traceability systems identified during our traceability audits. During some audits, samples could not be located or there was duplication of sample identifiers. Furthermore, inconsistent approaches to maintaining sample traceability were noted; for example, after an original piece of tissue had been divided to generate further samples.

84. During one inspection, multiple issues were identified with regards to the tissue traceability systems being used, which gave rise to a major shortfall. The establishment had in place a range of computer databases and spreadsheets across the hub and satellite sites. HTA audits performed during the inspection highlighted a need for tissue traceability to be strengthened. The issues identified were:

- the storage of some un-catalogued human tissue;
- some laboratory records did not capture sample identifiers;
- there were inconsistent approaches to recording traceability for samples released for research.

## Advice and learning: GQ6



85. Forty eight items of advice were given against standard GQ6.

86. A register of donated material should be maintained by the establishment for all human tissue stored under the licence. HTA-licensed establishments should be able to demonstrate their awareness of, and ability to track, ethical approval expiry dates.

87. Although human tissue samples were typically traceable during HTA audits, there were instances where it was difficult to obtain traceability information as it was not always readily available. Although samples could be located, the associated paper or electronic records were sometimes not easily accessible. Therefore, establishments should consider the methods used to store and retrieve records.

88. A few establishments were found to be storing 'existing holdings' of human tissue in the form of slides that had not been catalogued. Under the HT Act, existing holdings are exempted from the consent requirements; however, they must be stored under the governance of a HTA licence. All samples must be catalogued if they are to be stored on licensed premises for use in research.

89. Where discrepancies or transcription errors were identified during our traceability audits, advice was given to establishments about including a regular audit of records to ensure that errors are identified and corrected.

90. It is important that traceability records are created and maintained consistently by staff. Establishments are expected to have procedures that describe how each key component of the database should be populated. For example, establishments may also choose to use laminated work instructions located near work stations to enable staff to access this information readily.

91. Establishments may wish to set out agreements that make specific reference to all associated tissue samples received under the terms of the agreement along with their respective unique identifiers. Establishments used this approach to further strengthen tissue traceability.

### *GQ7 There are systems to ensure that all adverse events are investigated promptly*

92. Three minor shortfalls were identified against standard GQ7.

93. All shortfalls were attributed to the absence of documented procedures for handling adverse incidents as well as lack of suitable systems to allow adverse events to be formally captured.

## Advice and learning: GQ7



94. Twelve items of advice were given against standard GQ7.

95. Establishments need to have systems to record and manage adverse events. When an incident occurs, the HTA advises that establishments carry out a thorough investigation to establish the root causes and put in place CAPAs to prevent recurrences. We expect all HTA-licensed establishments to have a procedure in place for dealing with incidents involving human tissue samples.

96. Advice was given to establishments to carry out analyses of their adverse event data in order to better understand any trends and identify areas requiring improvement.

97. Under the Human Tissue (Quality and Safety for Human Application) Regulations 2007, serious adverse events and reactions must be reported to the HTA. On occasions, establishments have documented this reporting requirement in their SOPs, even though it is not relevant to research establishments licensed under the HT Act. Although there is no mandatory reporting system for notifying the HTA about adverse incidents in the research sector, establishments are encouraged to discuss their concerns with us, especially if they require further advice.

### *GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately*

98. This standard received the highest number of shortfalls, with twenty minor shortfalls and one major shortfall being identified.

99. The vast majority of minor shortfalls were due to a limited scope of risk assessments. Frequently, only risk assessments relating to health and safety risks were in place and there were no documented risk assessments associated with human tissue and licensed activities.

100. Risk assessments are a useful tool for establishments to assess which activities or areas pose the most risk. They also enable establishments to assess whether the control measures that have been implemented are adequate to reduce the likelihood of a problem occurring. Risk assessments should be regularly reviewed, especially when procedures or practices are subject to change.

101. One establishment was storing human tissue in multiple locations on its premises, some of which were un-catalogued tissue collections. A major shortfall was identified because tissue traceability systems were found to be unsatisfactory and there were no risk assessments covering tissue traceability.

## Advice and learning: GQ8



102. Fifty three items of advice were provided against standard GQ8; the highest number across the GQ standards.

103. Where establishments had risk assessments in place that covered some of the risks associated with their licensed activities, they were advised to extend the scope of their risk assessments to include other areas of risk, including:

- loss of traceability;
- loss of tissue;
- critical storage failure;
- missing or incorrect documentation;
- security arrangements;
- appropriate disposal.

104. Specific risks that were identified during inspections were routinely highlighted to establishments, in conjunction with providing advice to conduct a documented risk assessment.

105. By documenting risk assessments, staff are made aware of identified risks, which helps to prevent the risks materialising and informs the development of procedures and relevant documentation.

## Good practice: GQ1-GQ8



106. Established governance meetings, where matters relating to HTA-licensed activities could be discussed, were noted as good practice throughout a range of inspections. These meetings were often used effectively to discuss audits findings, SOPs, incidents and any other matters relating to licensed activities.

107. A comprehensive approach to audits, including those focussed on record completion, traceability and consent checks, was observed throughout inspections, together with a robust follow-up of actions arising from audits. Some establishments also had routinely adopted audits undertaken by external reviewers, in addition to their own internal audits.

108. SOPs and quality documents had typically been written to a high standard, with documented procedures made available for all licensed activities.

109. Several establishments were using effective traceability systems that were tailor-made to meet their needs as complex research tissue banks managing varied tissue collections. During our inspections, we noted several establishments who had adopted a unified approach to managing human tissue stored under the governance of NHS ethical approvals and human tissue stored under the HTA licence.

110. Although standard GQ8 was associated with the most advice, several establishments did have a good range of risk assessments identifying the key risks to human tissue.



# Premises, Facilities and Equipment standards (PFE1-PFE5)

## Key findings

111. The premises where licensable activities take place must be fit for purpose. The majority of premises were found to be suitable; however, there were weaknesses identified in areas relevant to security, monitoring of critical storage conditions, maintenance and servicing of equipment, and transport of tissue. Standard PFE3 received the highest number of advice items, relating to contingency arrangements, critical storage condition monitoring and alarm testing.

### *PFE1 The premises are fit for purpose*

112. Two minor shortfalls were found against standard PFE1.

113. A minor shortfall was identified at one establishment where a premises risk assessment for a proposed human tissue storage facility had not been undertaken.

114. A minor shortfall was identified at another establishment where the out-of-hours security arrangements were unclear because the information provided to security staff was inconsistent. There was ambiguity surrounding the responsibilities of security staff in relation to detected oxygen monitoring problems. In the event of an alarm, it was unclear if security staff would be required to call an engineer or visit the storage area to see if anyone needed assistance.

## Advice and learning: PFE1

115. Four pieces of advice were provided in relation to standard PFE1.

116. A premises risk assessment should take into consideration if the facility offers adequate space for licensable activities to be carried out and whether it is safe and secure for staff and human tissue storage.



117. Advice was given with respect to identifying an alternative suitable and appropriately licensed storage facility to store historical relevant material when future capacity became limited.

119. Establishments should carefully consider a 'no lone working' policy as well as the use of personal oxygen alarms to reduce the risks associated with working in a liquid nitrogen storage facility.

118. Security arrangements should ensure that areas where human tissue is stored are secure and restricted to authorised personnel.

120. Oxygen monitoring is extremely important for establishments to ensure that staff accessing human tissue stored in liquid or vapour phase nitrogen can do so safely. Such arrangements should be formalised, documented and provided to relevant staff.

### *PFE2 Environmental controls are in place to avoid potential contamination*

121. One minor shortfall was found against standard PFE2. In this case, there were no documented cleaning and decontamination procedures for the fridges and freezers used to store human tissue.

## Advice and learning: PFE2



122. Ten pieces of advice were given against standard PFE2.

123. Human tissue which poses infection risks may be stored by establishments. Where this is the case, establishments need to undertake risk assessments that include the risks to staff as well as the range of risks of storing human tissue which is infectious or of unknown infectious status.

124. Advice was given to one establishment about the management of risks associated with cross contamination between two areas on the same premises. Staff could move freely between the sample processing area and the human tissue archive area, and there was no demarcation to differentiate between 'clean' and 'dirty' areas.

## *PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records*

125. Four minor shortfalls were found against standard PFE3.

126. There were inconsistencies in the frequency of temperature monitoring of critical storage areas, and some establishments were not monitoring critical storage temperatures at all.

127. Inadequate security arrangements were identified at an establishment where human tissue was being stored in liquid nitrogen dewars and, although these were secured using padlocks, they were located in an unlocked shed outside of the main premises.

## Advice and learning: PFE3



128. Fifty six items of advice were given against standard PFE3, which is the highest number of advice items compared to all other standards.

129. Establishments need to have suitable and defined contingency arrangements in place. There were often additional fridges or freezers that could be used to store tissue in the event of a critical storage area failure. However, contingency arrangements had not always been formalised as a procedure or within an agreement.

130. Critical storage conditions need to be monitored and alarmed. Temperature monitoring of critical storage areas is important as it provides on-going assurance that equipment is functioning optimally and may help to identify any problems before equipment failure occurs. Furthermore a schedule of alarm testing ensures that they are functioning correctly.

131. Other items of advice related to ensuring that the premises and critical storage areas where relevant material is stored:

- are appropriately secured;
- have risk assessments for use of paper records in case of data loss;
- have suitable containers to store relevant material, which are fully labelled and are clear about containing human tissue.
- provide information about the alarm set points;
- provide advice to personnel about what to do if an alarm sounds.

## *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*

132. Three minor shortfalls were found against standard PFE4.

133. Where shortfalls were identified, there were no documented procedures to provide details about transportation of relevant material between establishments. In one specific case, the establishment had also not assessed the risks posed by their practice of encouraging staff to use their own vehicles to transport relevant material from other establishments to their premises.

## Advice and learning: PFE4



134. Two items of advice were provided against PFE4.

135. Even though one establishment was not transporting relevant material at the time of inspection, in anticipation of future planned activities, advice was given for policies and procedures to be reviewed, not least to ensure that they incorporated details about transporting relevant material.

136. Documented formal procedures for transporting human tissue samples may include information on:

- tissue packaging and labelling
- the responsibilities of staff organising transport
- maintaining traceability of tissue samples being transported
- the responsibilities of couriers collecting samples

137. Establishments should ensure that they have agreements in place with couriers responsible for transporting human tissue samples, so that each party understands their responsibilities with regard to maintaining tissue integrity and traceability.

*PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored*

138. Four minor shortfalls were found against standard PFE5.

139. Where shortfalls were identified, establishments did not ensure that equipment was subject to regular maintenance and servicing. Problems were identified where the maintenance contract for freezers had expired and there was no evidence of renewal.

## Advice and learning: PFE5



140. Thirteen items of advice were given against standard PFE5.

141. There should be routine maintenance and servicing of equipment, in accordance with the recommendations of the manufacturers.

142. Furthermore, establishments should ensure that scheduled calibration is documented and that labels are affixed to relevant equipment to provide evidence that annual calibration and maintenance has taken place.

## Good practice: PFE1-PFE5



143. Good practice was noted at one establishment which regularly and manually challenged the alarm system by creating out-of-limits temperature events, to ensure it was functioning as expected. Other establishments demonstrated robust temperature monitoring and trend analysis of data.

144. In the event of a mains power failure, two establishments had back-up arrangements for their fridges and freezers, in the form of a generator and carbon dioxide cylinders.

145. Robust, documented contingency and capacity arrangements were widely in place for establishments in the event that the fridge and freezer storage areas fail.

## Disposal standards (D1–D2)

### Key findings

146. Establishments demonstrated good compliance with the disposal standards, as indicated by the small proportion of shortfalls identified. The main gaps were due to lack of policies and procedures, or under-developed systems for recording disposal.

### *D1 There is a clear and sensitive policy for disposing of body parts and tissue*

147. Three minor shortfalls were identified against standard D1.

148. Where there were weaknesses, it was found that policies did not contain sufficient details about the sensitive disposal of human tissue. The policies tended to handle disposal of waste only and some establishments did not have a documented procedure in place for the disposal of human tissue.

## Advice and learning: D1

149. Seventeen items of advice were given against standard D1.

150. The most frequent advice given to establishments was about ensuring that clinical waste is bagged separately from human tissue. It is not necessary for each tissue sample to be bagged and disposed of individually.



## *D2 The reasons for disposal and the methods used are carefully documented*

151. Two minor shortfalls were found against standard D2.

153. During a traceability audit at another establishment, the reason, date and method of disposal for a sample had not been recorded.

152. One establishment had in place a suitable database to record sample disposal for human tissue; however, some locally-developed spreadsheets to record traceability for some tissue collections were not in line with the establishment's main system.

## Advice and learning: D2



154. Nineteen items of advice were given against standard D2.

155. The majority of establishments were advised to consider updating their SOPs, as well as reviewing their current databases, to ensure that they accurately reflected the reason, date and method of disposal of all human tissue samples.

156. For traceability to be maintained, systems should accurately reflect the fate of human tissue. This also includes whether it has been rendered acellular and if it has been used up during an experiment.

## Good practice: D1-D2



157. Overall, establishments had well-developed disposal SOPs and systems to capture traceability, from the point of human tissue sample receipt to disposal.

158. One establishment ensured that the traceability of expanded cells (which are not relevant material), from the point of expansion to disposal, was also being recorded. Similarly, aliquots of human tissue samples, from the point the aliquots were generated to the point of their disposal, were being documented using the traceability system.

159. Observed as good practice, some establishments were found to have adopted a uniform approach to recording traceability information which extended to samples which are not relevant material.



# Appendix 1: Licensing and inspection processes

## Inspections

We use the term 'inspection' to describe when we visit an establishment to meet with staff, view premises and facilities, and review policies and procedures.

We carry out inspections to assess if the Designated Individual (DI) is suitable to supervise the activity covered by the licence, as it is their responsibility to ensure that:

- other staff working under the licence are suitable;
- suitable practices are used when carrying out the activity; and
- the conditions of the licence are met.

We also need to be satisfied that the licence applicant or holder, the establishment's premises, and the practices relating to licensed activities, are suitable.

To help us reach our decisions, we have developed standards under four headings: Consent; Governance and Quality; Premises, Facilities and Equipment; and Disposal.

After every site visit inspection, we write a report documenting our findings. 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.

### **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

### **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 preventive 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.

### **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 preventive actions within 3-4 months of the issue of the final inspection report.

## Follow up actions

A template corrective and preventive action plan will be sent as a separate Word document with both the draft and final inspection report. The establishment 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 preventive 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 the establishment's proposed action plan, they are notified of the follow-up approach the HTA will take.

Reports for site visit inspections which have taken place since 1 November 2010 are published on our website.

## Appendix 2: List of establishments included in this report

Licence number	Establishment name	Satellites
12290	Alder Hey Children's NHS Foundation Trust	
12534	Newcastle University	<ol style="list-style-type: none"> <li>1. Institute of Genetic Medicine</li> <li>2. School of Agriculture, Food and Rural Development, Agricultural Building</li> <li>3. Institute of Neuroscience, Edwardson Building</li> <li>4. Freeman Hospital</li> </ol>
12515	Anglia Ruskin University	
12514	British American Tobacco Group Research and Development Centre	
12374	Vertex Pharmaceuticals (Europe) Limited	
12344	Source Bioscience PLC	
12384	University of Leicester	<ol style="list-style-type: none"> <li>1. Medical Research Council Toxicology Unit</li> <li>2. Glenfield General Hospital</li> </ol>
12122	Astex Therapeutics Limited	
12382	Durham University	1. Durham University (TS17 6BH)
12021	Liverpool Tissue Bank	
12508	University of Reading	
12277	Eastman Dental Institute	1. UCL Eastman Continuing Professional Development
12274	Prosidion Limited	
12572	Eurofins Pharma Bioanalysis Services UK Limited	
12326	Oxford Centre for Diabetes Endocrinology and Metabolism	
12252	Smith & Nephew Surgical Skills Centre	
12513	Quest Diagnostics Limited	
12443	BBI Solutions Sittingbourne	

12217	John Radcliffe Hospital	<ol style="list-style-type: none"> <li>1. Department of Pharmacology</li> <li>2. Nuffield Orthopaedic Centre</li> <li>3. Oxford Radcliffe Biobank, The Churchill Hospital</li> <li>4. Oxford Radcliffe Biobank, Cowley Store, University of Oxford</li> </ol>
12504	UCB Celltech	
12177	UCL Institute of Ophthalmology	
12321	National Institute for Biological Standard and Control	
12388	Royal Brompton and Harefield NHS Foundation Trust	<ol style="list-style-type: none"> <li>1. Imperial College School of Medicine, SW3 6LR</li> <li>2. Imperial College School of Medicine, SW3 6LY</li> <li>3. Imperial College School of Medicine, SW7 2AZ</li> <li>4. Harefield Hospital</li> </ol>
12419	Kingston University	
12119	The University of Sussex	
12378	King's College Hospital	
12335	St Georges University of London	
12115	The Grove Centre	
12276	Royal Devon and Exeter NHS Foundation Trust	<ol style="list-style-type: none"> <li>1. Royal Devon and Exeter Foundation Trust, Freezer Store</li> </ol>
12103	Peninsula Schools of Medicine and Dentistry	<ol style="list-style-type: none"> <li>1. University of Plymouth School of Biomedical and Healthcare Sciences</li> </ol>
12104	University of Exeter Medical School	<ol style="list-style-type: none"> <li>1. University of Exeter-Streatham Campus</li> </ol>
12402	Manchester Metropolitan University	<ol style="list-style-type: none"> <li>1. Manchester Metropolitan- Alsager Campus</li> </ol>
12583	School of Pharmacy and Biomolecular Science	
12352	St James University Hospital	<ol style="list-style-type: none"> <li>1. University of Leeds</li> <li>2. Chapel Allerton Hospital</li> </ol>
12097	HistologiX Limited	
12365	University of Surrey	<ol style="list-style-type: none"> <li>1. Postgraduate Medical School, University of Surrey</li> <li>2. Surrey Clinical Research Centre</li> </ol>
12585	Evotec UK Limited	

12533	Middlesex University	
30000	Royal Marsden Hospital	1. Royal Marsden Hospital, SM2 5PT
12558	Eli Lilly and Company Limited	
12084	Pfizer Limited (Neusentis Research Group)	
12322	The Institute of Cancer Research	1. The Institute of Cancer Research, SW3 6JB
12512	Oakfield House, School of Social and Community Medicine, University of Bristol	
12044	Queen's University Belfast	
12200	Bristol Dental School & Hospital	
12121	Guy's & St Thomas's Research Tissue Bank	1. GSTRB-St Thomas's Site
12030	The Walton Centre NHS Foundation Trust	
12074	Unilever Research and Development Port Sunlight	
12539	Oxford Biotherapeutics Limited	
12116	South Wing Proteomics Laboratory	
12590	Lonza Biologics Plc	
12610	PCI	1. Biotec 2
12600	LGC Genomics	
12400	Envigo Huntingdon	1. Envigo Shardlow 2. Envigo Eye
12528	Liverpool John Moores University	
12597	Fahy Gurteen UK Limited	
12588	ProImmune Limited	
12055	UCL Cancer Institute	1. Royal National Orthopaedic Hospital and UCL Institute of Orthopaedics 2. UCL Cruciform Building
12494	Covance Laboratories Limited	1. Covance Laboratories Limited, NE66 2JH
12594	Hvivo Services Limited	
12383	MRC Human Nutrition Research	
12584	GE Healthcare Cell Technologies	
12577	Loughborough University	
12510	Sequani Limited	
12613	Propath UK Limited	
12056	Lancashire Teaching Hospitals Foundation NHS Trust	
12563	Leica Biosystems Newcastle Limited	
12532	Synairgen Research Limited	

12283	MedImmune Limited	<ol style="list-style-type: none"> <li>1. MedImmune Limited, CB21 4AT</li> <li>2. MedImmune Limited, CB21 6GG</li> <li>3. MedImmune Limited, CB21 6GH</li> <li>4. Spirogen</li> </ol>
12614	Sygnature Discovery Limited	
12193	Newcastle Upon Tyne Hospitals NHS Foundation Trust	
12587	Imanova Limited	
12275	Hammersmith Hospital	<ol style="list-style-type: none"> <li>1. St Mark's and Northwick Park Hospitals</li> <li>2. South Kensington Campus</li> <li>3. St Mary's Hospital</li> <li>4. Charing Cross Hospital</li> </ol>
12059	Queen's University Belfast	
12559	Almac Diagnostics	
12198	University College London	<ol style="list-style-type: none"> <li>1. UCL Institute of Neurology</li> </ol>
12607	Pathology Diagnostics Limited	
12549	Quintiles Drug Research Unit at Guy's Hospital	<ol style="list-style-type: none"> <li>1. Quintiles Drug Research Unit at Guy's Hospital, SE1 9RT</li> </ol>
12240	MRC Clinical Sciences Centre	
12571	Oxford BioDynamics Limited	
12604	The University of York	
12586	OGT Limited	<ol style="list-style-type: none"> <li>1. OGT Limited, OX5 1PF</li> </ol>
12617	Re:Cognition Health Limited	
12611	Ipsen Bioinnovation Limited	
12381	Aston University	
12615	St Mary's University	
12598	Crown Bioscience UK Limited	