Site visit inspection report on compliance with HTA minimum standards

SPD Development Company Ltd

HTA licensing number 12636

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**

13 July 2016

Summary of inspection findings

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

Although the HTA found that SPD Development Company Ltd (the establishment) had met the majority of the HTA standards, three minor shortfalls were found with regard to the Governance and Quality Systems (GQS) standards. They were in relation to an absence of: (i) governance meetings; (ii) consistent reporting and follow up of adverse events; and (iii) risk assessments. Advice has been given relating to the Consent, GQS, Premises, Facilities and Equipment and Disposal standards, as well as to licence management.

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

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual (DI), Licence Holder (LH), premises and practices are suitable.

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.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. The HTA inspects the establishments it licenses against four groups of standards:

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

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

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by SPD Development Company Ltd (SPD, the establishment). SPD was issued an HTA licence in August 2015. The current inspection was the first routine site visit to assess whether the establishment is meeting the HTA's standards.

Swiss Precision Diagnostics GmbH was formed in 2007 as a joint venture between Procter & Gamble Co (P&G) and Alere Inc. The company is a supplier of home pregnancy and fertility/ovulation testing kits and conducts research in the area of reproductive health. SPD's headquarters are in Geneva, Switzerland and its UK subsidiary (SPD) has research and development laboratories situated in Bedford which accommodate approximately 35 staff.

The premises in Bedford are licensed under the Human Tissue Act 2004 (HT Act) for the storage of relevant material for use for a scheduled purpose. In this case, relevant material from living donors is being stored for the scheduled purpose of 'research in connection with disorders, or the functioning, of the human body'. The establishment is also storing relevant material from living donors for the scheduled purpose of 'performance assessment' but this is exempt from licensing. The DI supervising activities taking place under the licence is the Head of Regulatory, Clinical and Exploratory Medical Affairs; the Corporate LH (CLH) is SPD Development Company Ltd and the CLH Contact (CLHC) is the Research and Development Director.

SPD stores three sets of samples. One set (sample set 1: approximately 24,000 urine samples) has been obtained from women, including volunteer staff members, as part of national volunteer studies into assessing the performance of in vitro diagnostic testing kits in

analysing levels of hormones and other biomarkers related to women's health, pregnancy and fertility. The original consent given for the storage and use of these samples was for performance assessment, and SPD are now assessing whether to re-consent a cohort of such donors so that the samples can be used for research.

In relation to the second set (sample set 2: 800 urine samples), consent was also originally sought from national volunteers and staff members for performance assessment and the establishment is now actively approaching donors to re-consent for biomarker research studies. Separate research consent forms, approved by the establishment's ethics committee, are being used. The HTA has provided advice on this (*see Advice items 2 and 3*).

For sample sets 1 and 2 (above), consent is sought by SPD staff who have received consent training provided by the Clinical Programme Manager. Consent forms and participant information sheets are approved by the establishment's ethics committee. There is a standard operating procedure (SOP) for the seeking of consent and completed consent forms are held securely.

A third set of samples (sample set 3: 170 urine specimens) were originally obtained as part of an NHS Research Ethics Committee-approved study, which has now expired. The establishment is currently considering whether to re-consent the original donors for biomarker research studies.

The building is secure. The exterior is monitored by closed-circuit television (CCTV) and entry is restricted. Each laboratory is secured with both swipe card and key lock access.

Research samples are stored in two 4°C walk-in refrigerators and in two -80°C freezers. There is a separate -80°C freezer as a contingency. In addition, 22 (-80°C) freezers are used to store samples for performance assessment.

All refrigerators and freezers are linked to a continuous temperature monitoring unit feeding into a wireless callout system. This alerts the facilities staff, who relay the message to the relevant staff member. Temperature excursions outside the set ranges trigger audible alarms and the callout system but there are deficiencies in the system for identifying, recording and following up adverse events related to this process (*see Shortfall under GQ7*). The set range for the alarm system is not consistently documented and the callout system is not routinely tested (*see Advice items 4 and 10*).

Each sample is given a unique, bar-coded identification number, which is logged onto an electronic database. Both paper and electronic records are held securely.

The timetable for the site visit inspection was developed after consideration of information provided by the establishment at the time of its application for a licence, compliance update information and communications with the DI. The inspection included a visual inspection of the storage areas, discussions and interviews with key staff, and a review of documentation. Interviews were held with the DI, the Clinical Programme Manager, the Clinical Laboratory Manager and a Lead Scientist. Several audits of traceability were also carried out:

- The paper and electronic records of four separate specimens from sample set 2 were traced from consent to receipt, storage, use and disposal.
- Two specimens from sample set 3 were randomly selected from the -80°C freezer and labelling details were compared to paper and electronic records.

There were some discrepancies noted (*see Advice item 12*).

Inspection findings

The HTA found the DI and the CLH to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	There are no regular governance meetings where the DI, CLHC and - if appointed - Persons Designated (PDs) can discuss issues relating to HTA-licensed activities. In the context of the other identified shortfalls, these would help strengthen governance arrangements. *See Advice items 1 and 5.*	**Minor**
GQ7 There are systems to ensure that all adverse events are investigated promptly.	There is an inconsistent approach to identifying, recording and following up adverse events. During the inspection it was noted that the temperature of one of the refrigerators had exceeded the set point for a period of several days. Although this had been identified by facilities staff, there was a delay in transferring samples. This was not reported as an adverse event. *See Advice item 8*.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	There are health and safety risk assessments but there are no risk assessments relating specifically to the conduct of HTA-licensed activities. *See Advice item 9.*	**Minor**

Advice

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

No.	Standard	Advice
1.	N/A	The DI should consider appointing PDs to assist her in the role; the HTA should be notified of such appointments. Appointing PDs will clarify roles and responsibilities under the licence and will ensure that all licensed activities fall under the DI's supervision.
2.	C1	The HTA has given advice about the consent forms used for research. The DI may wish to review the consent form and consider whether generic consent would be more appropriate.

		The Health Research Authority (HRA) has produced a series of consent templates. The DI may wish to consider using these templates when creating a new consent form: http://www.hra-decisiontools.org.uk/consent/examples.html
3.	C2	The establishment's participant information sheets are general in their description of the use of donated samples. The DI may wish to consider revising the information available to donors to ensure that they are fully informed of the research uses to which their samples may be put. An HRA participant information sheet template is available: http://www.hra-decisiontools.org.uk/consent/examples.html
4.	GQ1	Labels on the freezers indicating set temperature ranges are inconsistent and out of date. One stated a temperature range of -60°C to -85°C and the other -70°C to -90°C. The DI should ensure that all SOPs, forms, labels and notices are updated and are included in the establishment's document control system.
5.	GQ1	In other establishments, governance meetings cover items such as standardisation of documents, changes to SOPs, audits and their findings, competence and regulatory training, management of incidents, risk assessments, the setting up of agreements with other establishments and the dissemination of national and local information relevant to activities in the research sector (for example, issues included in HTA e-newsletter items). The DI should ensure that the meetings are minuted and that actions are noted and followed up. Documented minutes should be distributed to all relevant staff.
6.	GQ3	The DI may wish to consider including online training packages as part of the staff training programme. One example is the MRC 'Research and Human Tissue Legislation e-learning Module', part of the MRC Data and Tissues Toolkit (both of which were developed with input from the HTA): www.rsclearn.mrc.ac.uk/.
7.	GQ4	The DI should ensure that all relevant staff have access to the electronic database.
8.	GQ7	All establishments licensed by the HTA are required to have an internal system for reporting adverse events and, where necessary, instigating an investigation or root cause analysis. The DI should ensure that staff are aware of incidents relating to human tissue. These include: • specimen loss • loss of specimen integrity (e.g. broken packaging) • missing, incomplete or incorrect documentation • refrigerator and freezer temperature warming or breakdown • incorrect disposal • breach of security.
9.	GQ8	As well as health and safety issues, the DI should also assess risks associated with licensed activities. These include:

		• loss of or damage to specimens • loss of traceability • receiving specimens without appropriate documentation • storage of specimens and contingency arrangements • transport of specimens to the establishment • disposal arrangements • security arrangements. Risk assessments should be reviewed regularly and after changes to key procedures. They should be made available to all staff undertaking licensed activities.
10.	PFE3	The DI should carry out regular testing of the continuous temperature monitoring system to ensure that the callout procedure is functioning correctly.
11.	PFE3	The DI may wish to consider initiating a program by which, at suitable timeframes, the temperature plots from the monitoring system are reviewed. This may help to identify a potential failure of the system before it occurs.
12.	D2	The DI should ensure that the reason for disposal of samples is recorded and that this change in practice is included in the appropriate SOP(s). The DI should ensure that disposal details (date, method and reason) are included in the electronic database.

Concluding comments

During the inspection areas of good practice were noted:

- All staff receive consent and regulatory training (including training on the HT Act and the HTA's Codes of Practice). A centralised log of this training is kept and refresher training is provided on a regular basis.
- The establishment has a formal system whereby only qualified staff auditors can take part in the internal audit schedule. This ensures consistency of practice.

There are a number of areas of practice that require improvement, including three minor shortfalls. The HTA has given advice to the DI with respect to the Consent, Governance and Quality Systems, Premises, Facilities and Equipment and Disposal standards, as well as to licence management.

The HTA requires that the DI addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 03 August 2016

Report returned from DI: 15 August 2016

Final report issued: 14 September 2016

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: 01 June 2017

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below. 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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training

- Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes • Complaints system
GQ2 There is a documented system of quality management and audit
• A document control system, covering all documented policies and standard operating procedures (SOPs). • Schedule of audits • Change control mechanisms for the implementation of new operational procedures
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
• Qualifications of staff and training are recorded, records showing attendance at training • Orientation and induction programmes • Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training • Training and reference manuals • Staff appraisal / review records and personal development plans are in place
GQ4 There is a systematic and planned approach to the management of records
• Documented procedures for the creation, amendment, retention and destruction of records • Regular audit of record content to check for completeness, legibility and accuracy • Back-up / recovery facility in the event of loss of records • Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail
• There is an identification system which assigns a unique code to each donation and to each of the products associated with it • An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom
GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination • Appropriate health and safety controls are in place

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.
• Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination • Contingency plans are in place in case of failure in storage area • Critical storage conditions are monitored and recorded • System to deal with emergencies on 24-hour basis • Records indicating where the material is stored in the premises
PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination
• Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation • A system is in place to ensure that traceability of relevant material is maintained during transport • Records of transportation and delivery • Records are kept of any agreements with recipients of relevant material • Records are kept of any agreements with courier or transport companies
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored
• Records of calibration, validation and maintenance, including any agreements with maintenance companies • Users have access to instructions for equipment and receive training in use and maintenance where appropriate • Staff aware of how to report an equipment problem • Contingency plan for equipment failure

Disposal Standards
D1 There is a clear and sensitive policy for disposing of human organs and tissue
• Documented disposal policy • Policy is made available to the public • Compliance with health and safety recommendations
D2 The reason for disposal and the methods used are carefully documented
• Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal

- Where applicable, disposal arrangements reflect specified wishes

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 inspection.

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

Follow up actions

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

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

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

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