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QUALITY MANUAL

ISO15189:2012

13th July 2020

This document, together with specified procedures, represents the Quality Management System of Micropathology Limited. It has been compiled to meet the United Kingdom accreditation service requirements of a Quality Management system and appropriate national and international standards including ISO15189:2012.

Reviews

First edition – 23rd January 2017.
Revision – 17th February 2017. Minor formatting to headings.
Revision – 22nd March 2017 - Addition of new format of the floorplan.
Revision – 27th March 2017 – changed date on front page from February to March
Revision – 26th June 2017 – Reworked organisational chart, communication details updated, additional details added regarding the handling of user feedback.
Revision – 28th January 2018 – New company floor plan added. Updated responsibility, authority and inter-relationships section. Updated Selection, verification and validation of examination procedures section
Revision – 15th March 2018 – Updated job descriptions in the responsibility, authority and inter-relationships section.
Revision 29th June 2018. Update Quality policy to detail ongoing review of objectives and discussion in the Annual Management review. Addition of Companies house registration number in the legal entity section. Change of title from Dr. to Prof. for Prof. Fink throughout the document. Addition of User feedback and complaints SOP reference in needs of users section. Addition of Quality indicators and auditing meeting in communication section. Detail that Micropathology Ltd no longer refer samples to other laboratories. Risk Management added to SOP reference for Identification and control of non-conformities in section Evaluation and audits. Details of inter-operator competence schemes added to competency section. Extracted nucleic acid storage added to storage facilities section. Extra worksheet reference added to examination validation / verification processes section. Location of equipment manuals for use amended. Details of signing for acceptability of equipment post service / repair added to equipment records section. Details of the education information sheets added to the information for users section. Minor formatting to headings throughout the document.
Revision April 2019 – Update of floor plan following addition of new unit. Update of SOPs and associated title references throughout. Update of organisational plan due to new member of staff. Update of job descriptions list. Type of meetings held updated throughout. Addition of new role, Consultant Microbiologist / Virologist in responsibilities section.
Revision 24-4-2019 – Add consultant virologist / microbiologist job description reference and update of laboratory directors section 4.1.1.4.
Revised 7th May 2019 – Alteration to Quality assistant job title in organisational chart.
Revised 3rd June 2019- amended typo in word ‘validation’ on page 29 and included reference to EQA procedures for QCMD, NEQAS and INSTAND under section 5.6.3.
Revised 1st July 2019 – Update of organisational chart. Addition of Software developer and administration and accounting job role to section 5.1.3. Corrected typo in revision on 3rd June 2019. Details of the ethical conduct form are added to section 4.1.1.3.
Revised 14th July 2019 – Change of Software developer role title to IT systems architect in section 5.1.3, and organisational chart.
Revised 3rd October 2019 – Add job description M-1683 to section 5.1.3. Removal of inter-laboratory exchange form reference and addition of EQA analysis form (QCMD/NEQAS) in 5.6.3.4. Addition of ethical conduct an conflict of interest details in the induction sections 5.1.4. Update of section 4.1.2.6 to better reflect timing of meetings and signing to agree minutes. Organisational chart updated to reflect types of scientists, senior scientists are responsible for.
Revised March 2020 – Removed the references to paternity testing. Updated Quality policy and job descriptions and research sections. Updated reference to HCPC registration in personal qualifications section. Updated research activities in responsibilities, authority and interrelationships section. Added extra details about temperature monitoring in fridges and freezers in reagents and consumables section. Addition of SOP ‘Additional test requests’ to request form

information section. Removed the reference to the QCMD score cards in the interlaboratory exchange section. Updated the information of users section to reflect current practice. Updated Information Systems Management SOP reference.
13th July 2020 – Update company floor plan. Removal reference to sending postal copies of reports as this is no longer performed. Addition of facilities maintenance and environmental conditions SOP in 5.2.6 and 5.6.1. Added the in-house database details to section 5.3.2.

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GENERAL INFORMATION

Title of Laboratory

The laboratory is a part of Micropathology Limited, an independent research and diagnostic service provider.

Information on the services provided is available on the company's website (http://www.micropathology.com/) from where the Laboratory User Handbook (also held on iPassport for internal use) can be downloaded.

The routine diagnostic work of the company comprises of the molecular diagnosis of infectious diseases, genetic disorders, identification of human remains and familial relationship testing. In addition to these services the laboratory also undertakes a variety of research and contract testing activities and supports post-graduate research with other institutions.

The Quality Manual

This Quality Manual describes the Quality Management System (QMS) of Micropathology Limited for the benefit of the management and staff of the company and provides information for inspection or accreditation bodies. It contains references to the ISO15189:2012 standard and to procedures written in fulfilment of these standards.

The sections of this Quality Manual are arranged to equate with the ISO15189:2012 standard. The title of each clause / subclause is accompanied by a brief description of how Micropathology Limited seeks to comply.

The Quality Policy of Micropathology Limited

Scope of the service:-

Micropathology Limited specialises in using the latest molecular techniques to provide a clinically supported service for rapid diagnosis and management of infectious and genetic disease. We also provide a human genetic profiling for relationship testing and human identification genetics service. Our staff undertakes biomedical research covering human and veterinary pathology. This includes contract research and clinical trials for external organisations, in concert with continuous in-house assay development.

The directors and staff of the company strive to provide the highest possible standards in all aspects of the company's activities. We welcome a continuing dialogue with our clients in any aspect of clinical diagnostic testing.

In order to provide these services, which meet or exceed the needs and requirements of its users and patients, the laboratory management team is fully committed to:

Providing the highest quality analytical pathology service by:-

- Upholding professional values and continuing commitment to good professional practice and conduct.
- Staff recruitment, training, development and retention at all levels to provide a full and effective service to its users.
- Ensuring the use of examination procedures used is the highest achievable quality and they are fit for intended use.
- Procuring and maintaining the most appropriate equipment and resources to enable the provision of quality examinations of specimens.
- Giving advice on the collection and handling of all diagnostic samples, (to minimise uncertainty of results), allowing the production of quality assured results in a timely, confidential and clinically useful manner.
- Ensuring laboratory staff are familiar with the contents of this Policy, the Quality Manual and all procedures relevant to their work.
- Regular assessments of the satisfaction of users and staff. (E.g. by feedback from meetings, service updates, Christmas letters and user information sheets).
- Participation in internal audit schemes.
- Participation in National and European standards of excellence relevant to our clinical diagnostic work.
- Compliance with all relevant local and national legislation, including environmental legislation.

Achieving continual quality improvement in all areas of the laboratory by:-

- Continually developing the Quality Management System to allow improvements to all elements of the diagnostic Service.
- Annually reviewing the performance of company over the previous year and subsequently setting quality indicators, objectives and plans for the future, which will be implemented to comply with this Quality Policy. These Quality Objectives are set at the Annual Management Review and are reviewed monthly at general laboratory meetings for progress.
- Following Caldicott principles and complying with the standards set by external organisations, e.g. ISO15189:2012, Health and Safety Executive, Human Tissue Authority.
- Regularly reviewing the effectiveness of the Quality Management System through regular internal auditing.

The health, safety, welfare and development of all Micropathology Ltd staff by:-

- Ensuring a friendly working environment to encourage the retention and recruitment of highly professional staff, committed to excellent professional practice.
- Regularly reviewing, by audit and inspection, compliance with the Department's health & safety procedures.
- Analysing incidents, complaints and accident reports, applying remedial, corrective and/or preventative actions as appropriate and reviewing these actions for effectiveness.
- Providing resources for training, education and development for all staff.

Treating all visitors and callers to the Department with courtesy and respect by:-

- Being helpful and polite and giving consideration to their health, safety and welfare whilst in the laboratory and office facilities.

4 MANAGEMENT REQUIREMENTS

4.1 Organisation and Management Responsibility

4.1.1 Organisation

4.1.1.1 General

Micropathology Ltd shall meet the requirements of ISO15189:2012 when performing work at the laboratory and office facilities.

4.1.1.2 Legal Entity

Micropathology Ltd (Company registration number 3022426) is the sole entity legally responsible for the diagnostic activities performed on site.

4.1.1.3 Ethical conduct

All permanent staff enter into a formal employment contract. Activities not permitted at Micropathology Ltd, which could lead to a diminish in laboratory competence, impartiality, judgement or operational integrity are documented in the following sections: General terms of employment, Whistle blowers, Rights of Search, Confidentiality and Non-solicitation of the employee handbook. This forms part of the employee contract.

Such activities may also be detailed on the ethical conduct form S-1693-n.

All staff are bound by the terms of a confidentiality agreement, S-483-n.

All samples are treated in accordance with documentation: Guidance on the Use of Clinical Samples Retained in the Pathology Laboratory, M-176-n, The retention and storage of pathological specimens and records (5th edition) M-175-n and Procedure for the Control of Clinical Material S-178-n.

4.1.1.4 Laboratory director

Prof. Colin Fink, the laboratory medical director, and Dr Mark Atkins, Consultant Medical Virologist Microbiologist are Fellows of the Royal College of Pathologists. Prof. Fink maintains ultimate responsibility for the overall operation and administration of the laboratory. Prof. Fink and Dr Atkins are both responsible for directing the clinical diagnostic work and act in the manner of a Caldicott guardians. The duties and responsibilities are detailed in the relevant job descriptions as detailed in M-479-n and M-1607-n.

4.1.2 Management responsibility

4.1.2.1 Management commitment

Micropathology Limited will operate a Quality Management System (QMS), which will integrate the organisation procedures, processes and resources of the laboratory. Staff are responsible for ensuring the establishment, implementation and maintenance of the QMS.

4.1.2.2 Needs of users

Micropathology Limited keep in touch with users by i) informal/formal telephone conversations between staff members and clients, ii) visits and telephone calls made by the company representative, iii) emails to info@micropathology.com and iv) company website. The information gathered may be discussed at Laboratory / section meetings. The company representative writes informative notes detailing all communication held with the users via email, telephone or formal visits. These are available on iPassport.

User feedback is collated as detailed in the procedure Management of complaints and user feedback (S-1078-n) and logged in a customer spreadsheet. Complaints are also recorded directly onto the Non-compliance iPassport Database as detailed in S-1078-n. These maybe discussed at Laboratory and or Quality meetings.

Micropathology Limited ensures it provides the necessary equipment; environment and staff resources to ensure the needs and requirements of users are met. Requirements for additional equipment and resources are subject to discussion amongst staff and subsequently with the company directors or in a laboratory meeting.

Micropathology Ltd has a Business Contingency plan (S- 259-n) to ensure in the event of unforeseen circumstances, the needs and requirements of users are still met.

Micropathology Limited provides routine diagnostic work on an ad-hoc basis. When necessary, Micropathology Limited may enter into a formal Service level agreement as detailed in the ‘Procedure for the establishment and review of service level agreements- SOP S-633-n.

Documents pertaining to testing of patient samples and all related equipment maintenance records and calibrations are kept in accordance with the procedure S-177-n.

4.1.2.3 Quality policy

Laboratory management have produced a Quality policy for Micropathology Ltd. This is detailed on page 6/7 of this Quality Manual.

4.1.2.4 Quality objectives and planning

The laboratory management team defines and communicates the quality objectives of the laboratory in consultation with the staff and is responsible for ensuring that plans are made to meet these objectives. Quality objectives are subject to discussion in laboratory meetings, and may if required, be subject to amendment. The annual management review determines whether the objectives have been successfully completed and provides an opportunity for revising them.

The laboratory management have a document 'Quality indicators' (S-640-n), which details methods used to monitor quality improvement processes in the pre-examination, examination and post-examination areas of the laboratory.

The laboratory management have a procedure Change Control (S-1099-n) to ensure appropriate change management to enable the integrity of the Quality Management System to be maintained during periods of change.

The change control request form (S-1098-n) serves to monitor change within the company premises.

4.1.2.5 Responsibility, authority and interrelationships

Staff may have more than one role. Job descriptions are retained in each individual's training record folder or, in the case of the directors, the personnel file. Individual staff member's terms and conditions of service (contracts of employment) are retained by Management in the personnel file.

The laboratory have documented defined training programmes to ensure all staff are competent to perform their assigned duties.

Staff responsibilities are detailed in job descriptions, which are based on the templates:

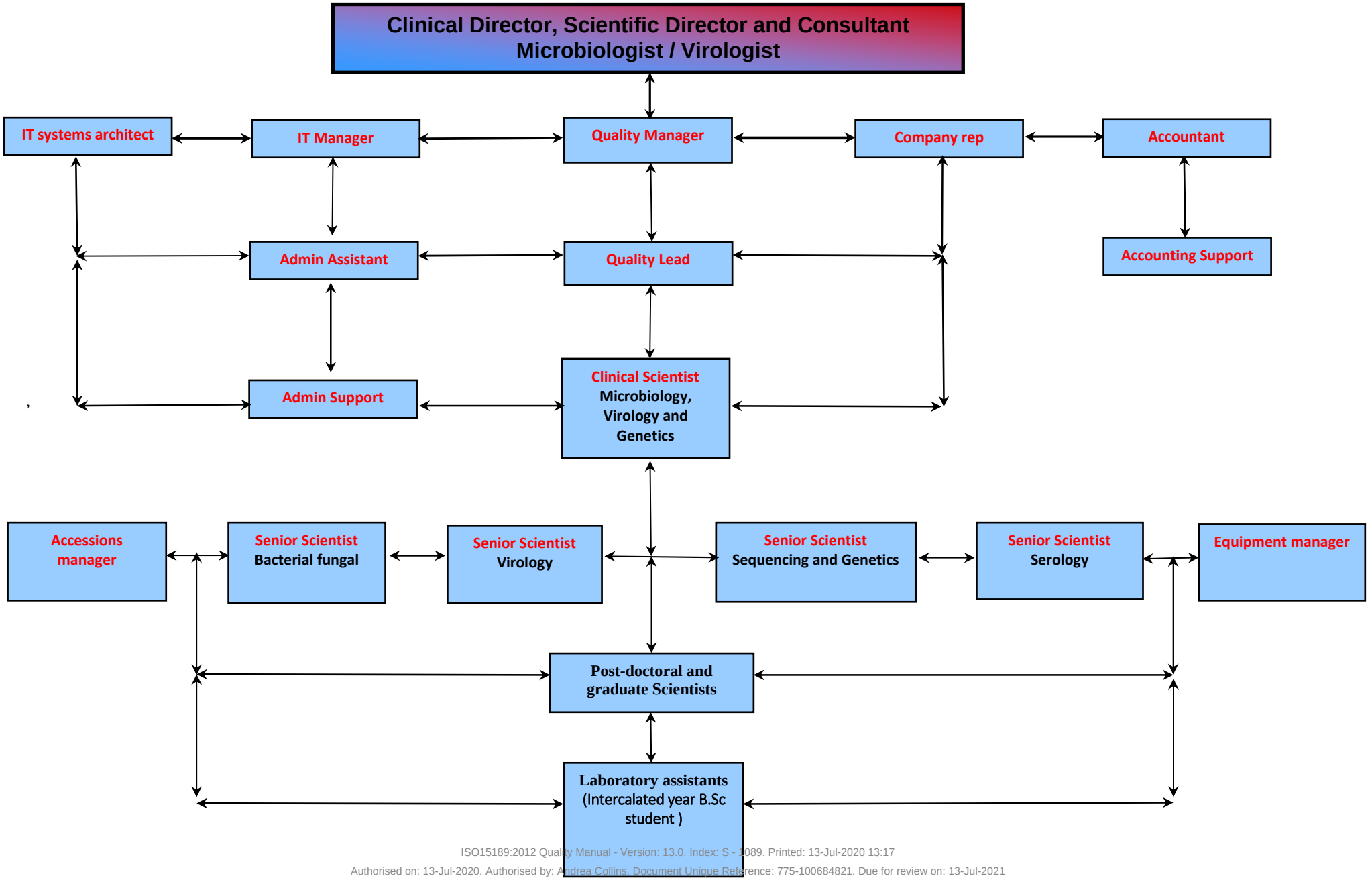
Scientist - M-129-n
Scientific Director - M-130-n
Company Representative - M-191-n
Fire warden – M-263-n
Company Accountant - M-298-n
Medical Director M-479-n
Laboratory Office Admin Assistant - M-480-n
Clinical Scientist - M-481-n
Quality Manager M-482-n
Laboratory Assistant intercalating year students - M-619-n
Health and Safety Co-ordinator - M-622-n
Training Officer - M-623-n
Post-doctoral Scientist – M-666-n
Post-doctoral Scientist with research responsibilities M- 1377-n
Post-doctoral Scientist with equipment responsibilities M- 1487-n
Quality lead M-1504-n-n
Research scientist M-1385-n
Administration support M-1390-n
Consultant Medical Virologist Microbiologist M-1607-n
Post-doctoral scientist with microbial genomics responsibilities M-1683-n
Post-doctoral project lead with Quality Assurance responsibilities M- 1826

Equipment Manager M-928 –n
Accessions Manager M-1053-n
Virology Manager M –1054-n
Sequencing Manager M-1055-n
Microbiology Manager M-1056-n
Serology Manager M-1061-n
Information Technology Manager M-1100-n
Laboratory Manager M-1518-n
Administration and accounting support M-1689-n
IT systems architect M-1692-n

Inter-relationships are defined in the figure on page 13. This figure solely represents how information related to the Quality Management System is transmitted.

There are currently two company directors (Clinical and Scientific) and a Consultant microbiologist / virologist who are aided by three HealthCare Professions Council state-registered Clinical Scientists (Molecular geneticist, Microbiology and Virology). They in turn are aided by a number of post-doctoral or post-graduate scientists, two of whom are registered with the IBMS as Biomedical Scientists. The company also employ a HealthCare Professions State Registered Clinical Scientist as the Company Representative, an accountant and several workers who provide administrative assistance.

Micropathology Ltd staff are also involved in lecturing on the degree courses within the Life Sciences / Medical School departments at the University of Warwick. The company also hosts intercalating year students from the University of Warwick.



Micropathology Ltd supports infectious disease and microbiological research through many academic partnerships and collaborations. As members of three international research consortia, we provide high-throughput diagnostic screening for research cohorts from across Europe and Africa:

PERFORM (EU Horizon 2020 grant agreement No. 668303)
DIAMONDS (EU Horizon 2020 grant agreement No. 848196)
UK Lead: Imperial College London
FIEBRE (Funded by UK aid from the UK government)
UK lead: London School of Hygiene and Tropical Medicine

Micropathology Ltd are also involved in a Metagenomic analysis of the microbiome in Kawasaki Disease, in collaboration with Imperial College London and the Academic Medical Centre, Amsterdam. Additionally, a phylogenetic study of the domestication of swiftlets, in collaboration with the University of Utara, Malaysia and Dr Gathorne Gathorne-Hardy (Lord Cranbrook), a tropical biologist and honorary research fellow, is currently in progress.

4.1.2.6 Communication

Main laboratory meetings are held approximately once a month to allow a formal exchange of information. These are chaired by the Quality Manager and all contracted members of staff are required to attend. These meetings follow an agenda and are minuted.

Additionally, the Quality Manager chairs Quality Indicators and Auditing and Strategic planning meetings for the review of the laboratory quality indicators, recent audits and issues regarding planning and laboratory moves. These meetings follow and agenda and are minuted. Laboratory staff also hold mini-meetings on an ad-hoc basis within defined laboratory sections (Microbiology, Virology, Serology and Sequencing). These meetings are chaired by the section head and follow an agenda. All meetings are minuted.

Signed copies of the minutes of meetings are held on iPassport under Laboratory Management > meetings for all members of staff, including those not present at the laboratory meeting itself.

4.1.2.7 Quality Manager

The laboratory management has appointed a Quality Manager. The Quality Manager reports directly to the management team and fulfils the role by; ensuring that the quality

management system (QMS) is implemented and maintained, reporting to the laboratory management on the functioning and effectiveness of the QMS, educating the staff in quality principles and practice, and coordinating the needs and requirements of users.

4.2 Quality management system

4.2.1 General requirement

The laboratory management have established a Quality Management System, the details of which are outlined in this Quality Manual. All staff are involved in continually monitoring its effectiveness in accordance with this standard.

4.2.2 Documentation requirements

4.2.2.1 General

The Micropathology Ltd QMS documentation includes:

- A Quality Policy (page 6/7)
- Quality objectives, which are updated in on annual basis and are included in the Annual Management review (M-583-n).
- The production of this Quality Manual (S-1089-n), written procedures and records as required by this International Standard.
- Documents and records determined by Micropathology Ltd staff essential in ensuring the effective planning, operation and control of the processes.
- Copies of all external regulations and standards which staff should be considerate of in their work.

4.2.2.2 Quality Manual

This Quality Manual describes the Quality Management System (QMS) of Micropathology Limited for the benefit of the management and staff of the company and provides information for inspection or accreditation bodies. It contains references to ISO15189:2012 standard and to procedures written in fulfilment of these standards.

The sections of this Quality Manual are arranged to equate with the ISO15189:2012 standard. The title of each standard is accompanied by a brief description of how Micropathology Limited seeks to comply. New editions are circulated amongst the staff to keep them informed and up-to-date**.**

4.3 Document Control

The laboratory management have established a procedure, Document control, (S-1-n), which controls all internally and externally generated documents relevant to the establishment, maintenance and improvement of the Quality Management System.

4.4 Service level agreements

The laboratory has established a document for the establishment and review of service level agreements for the provision of medical laboratory services (S-633-n)**.** Every request received by Micropathology Ltd is an agreement to perform a diagnostic service, where relevant and appropriate.

Please also refer to the section Selection, verification and validation of examination procedures (page 29 of this Quality Manual).

4.5 Examination by referral laboratories

Micropathology do not routinely refer specimens to other laboratories. If necessary samples can be sent for referral according to the procedure are handled using the procedure 'Examination by referral laboratories and sending samples to other laboratories' (S-11-n).

4.6 External services and supplies

The laboratory have established procedures for the selection and purchasing of external services, supplies, equipment, reagents, consumables that may affect the quality of its service. This is detailed in the procedure 'Procurement and Management of equipment, S-186-n and Reagents and consumables S-192-n.

4.7 Advisory services

The laboratory has established methods for communication with users.

Information is available on the company's website (http://www.micropathology.com/) from where the Laboratory User Handbook (S-748-n), sample request forms and information sheets can also be downloaded.

Details for contacting the laboratory are available on the company website and in the laboratory user handbook. The company also employs a company representative, who, continues to visit and telephone clients regularly and provides feedback, via written report, on their satisfaction with the service, any suggestions for improvement, any complaints and any requests they might have.

The laboratory management have established a procedure for the provision of clinical advice and interpretive comments. See S-13-n, Clinical Advice, Authorising and out of hours service.

Clinical and laboratory staff consult on the effective provision of services at laboratory meetings (see section 4.1.2.6 or further details).

Staff may alert users to scientific and logistic issues with samples by telephone, fax or email communication. Staff may also indicate any issues by way of a caveat or interpretative comments on reports**.** Clinical and laboratory staff consult on the effective provision of services at laboratory meetings.

4.8 Resolution of complaints

The laboratory Management have established a procedure for the management of complaints and other feedback received from clinicians, laboratory staff, and other parties (S-1078-n). Records of such communications are kept and are acted upon if required.

4.9 – 4.11 Identification and control of non-conformities, corrective action and preventative action

The laboratory management has established procedure for the identification and control of non-conformities and the implementation of corrective and preventative action (Identification and control of non-conformities, S-572-n).

4.12 Continual improvement

The laboratory management has an established procedures; Procedures for evaluation and improvement processes (S-187-n) and Quality Indicators (S-640-n) for continual improvement.

4.13 Control of Records

The laboratory management have established a procedure, S-177-n, for the Control of Records. Documents amendments are in accordance with the procedure 'Document control' S-1-n.

The company is registered as a data controller with the Information Commissioner's Office. Prof. Colin Fink and Dr Mark Atkins act in the manner of Caldicott guardians.

4.14 Evaluation and audits

The laboratory management have established procedures Quality Indicators (S-640-n), Procedure for evaluation and improvement (S-187-n), Identification and control of non-conformities and risk management (S-572-n), Inter laboratory comparisons (EQA) (S-531-n) and Auditing (S-168-n)) for:

a) Periodic review of requests, suitability of procedure and sample requirements (4.14.2)
b) Assessment of user satisfaction and complaints (4.14.3)
c) Staff suggestions (4.14.4)
d) Internal audit (4.14.5)
e) Risk Management (4.14.6)
f) Quality Indicators (4.14.7)
g) Reports from external assessments bodies (4.14.8)

To demonstrate that:

- The Quality Management System is being conducted in a manner that meets the need and requirements of users;
- There is conformity to the QMS;
- Continual improvement of the QMS and improved effectiveness.

Additionally, all items may be subject to discussion in various types of laboratory meetings. All meetings are minuted and minutes distributed to all staff.

The results of the evaluation and improvement processes are included in the input of the annual management review (4.15.4).

4.15 Management review

The laboratory management review the QMS at yearly intervals (4.15.1). The following items of information are considered (4.15.2);

a. Periodic review of requests, suitability of procedure and sample requirements
b. Assessment of user satisfaction and complaints
c. Staff suggestions
d. Internal audit
e. Risk Management
f. Use of Quality indicators
g. Reports of assessments by external organisations
h. Interlaboratory comparison programme reports
i. Monitoring and resolution of complaints
j. Performance of suppliers
k. Identification and control of non-conformities
l. Results of continual improvement
m. Follow up of previous management reviews.
n. Major changes in organisation and management, resource (including staffing) or process
o. Recommendations for improvement, including technical requirements.

The review also includes information regarding the causes for non-compliances within these sections and details any noticeable trends / patterns that may indicate a process problem (4.15.3).

Key objectives for the subsequent year are defined and plans formulated for their implementation. Records are kept and an executive summary is sent to UKAS (4.15.4).

5 TECHNICAL REQUIREMENTS

5.1 Personnel

5.1.1 General

The laboratory management have established a procedure, S-182-n (Procedure for personnel management), which allows staff to contribute fully and effectively to the service and receive fair and consistent treatment from laboratory management.

5.1.2 Personnel qualifications

Details of staff personal qualifications (CVs and copies of relevant degree certificates) are kept in the confidential personnel folder. Copies of IBMS / RCPath registration certificates are kept in the individuals training record folder. Staff registered by the HCPC can be checked on the HCPC website https://www.hcpc-uk.org

5.1.3 Job descriptions

Job descriptions are based on the templates as detailed in section Responsibility, authority and inter-relationships (Page 10 of this Quality Manual). Copies are retained in each individual's training record folder or, in the case of the directors, the personnel file.

Individual staff member's terms and conditions of service (contracts of employment) are retained by Directors in the confidential personnel folder. The confidential personnel folder also contains sickness and absence records, and occupational health records.

5.1.4 Staff induction and training

New personnel go through a staff orientation and induction process (S-30-n Induction and S-598-n, Induction record) which includes an assessment of ethical conduct (S-1693-n). Following completion of this, staff follow a supervised induction process followed by SOP-based training in all relevant aspects of their routine diagnostic work (see Training policy and competency assessment M-54-n, Training record form S-587-n and Personal Training Programme M-199-n). The training officer oversees this process. Records of the induction process and training are retained in each individual's personnel file and training record folder respectively.

Following the period of SOP-based training, other training resources are available: Micropathology Limited subscribes to a variety of journals and is a corporate member of the University of Warwick Library. All members of staff have access to the Internet. Micropathology Ltd. also hold in-house Journal Clubs; internal staff and external speakers may be invited to present and all staff are encouraged to participate. Personnel are encouraged to attend relevant meetings and conferences. Funding (to cover society membership, travel, conference fees, expenses) is provided by arrangement with the directors.

Micropathology Limited is a registered Institute of Biomedical Science Training laboratory. Staff may undertake the necessary training to qualify as a Biomedical Scientist.

Training and competency, copies of registration certificates and Continuing Professional Development are kept in the individual's training folder.

The Health & Safety Co-ordinator keeps records of attendance at fire safety training, manual handling training sessions and confidential records of accidents.

5.1.6 Competence

Competency is individually tailored for each staff member as detailed in M-54-n Training policy and competency assessment.

Staff are also subject to witness audits as detailed in the procedure 'Auditing' S-168 and are involved in participation in EQA (Inter laboratory comparison S-531-n) and IQA (IQA list S-273-n) schemes to demonstrate competence and inter-operator comparability schemes (S-1256-n, S-1270-n, S-1356-n).

5.1.7 Review of staff performance

Staff annual joint reviews are carried out according to the procedure Appraisal (S-128-n). Prof. Colin Fink keeps confidential records of staff annual joint reviews

5.1.8 Continuing professional development

All personnel are encouraged to keep records of continuing professional development and these are kept electronically or in personal or training record files for each individual.

5.1.9 Personnel records

Job descriptions, training and competency, copies of registration certificates and Continuing Professional Development are kept in the individual's training folder.

The confidential personnel folder contains records of induction, CV's, copies of degree certificates, terms and conditions of employment, sickness and absence records, conflict of interest records and occupational health records / records of accidents.

The Health & Safety Co-ordinator keeps records of attendance at fire safety training, manual handling training sessions and visual display equipment assessments.

Prof. Colin Fink keeps confidential records of staff annual joint reviews.

5.2 Accommodation and environmental conditions

5.2.1 General

Micropathology Limited occupies several combined units within The Venture Centre on the University of Warwick Science Park. A floor plan of Micropathology Limited is provided in Appendix 1.

5.2.2 Laboratory and office facilities

The Venture Centre provides a secure working environment. All visitors must first sign in at the reception desk and there is a security presence at night, during weekends and Bank Holidays. Micropathology Limited has its own security system, including electronic door locks and an intruder alarm. Key coded electronic locks protect all entry and exit doors.

Medical information, patient samples and laboratory resources are safeguarded from unauthorised access in accordance with the procedures 'Control of records (S-177-n) and Control of clinical material (S-178-n).

5.2.3 Storage facilities

Records:

Current process and quality records are stored electronically in the QMS iPassport. There is adequate storage space for the retention of paper records, as appropriate. Archived paper copies may be scanned to the Company server and stored for reference.

The laboratory management have established a procedure, S-177-n, for the Control of Records.

Experimental data results are stored electronically on the server and are backed up in accordance with above procedure (S-177-n). Patient records are stored electronically on the LIMS.

Clinical material:

Fridges and freezers are available for the storage of clinical material. Clinical samples are archived in numbered boxes kept at -20ºC. The laboratory management have established a procedure, S-178-n, for the Control of Clinical Material detailing the storage of these samples.

Extracted nucleic acids

Specimen extracts are available for repeat testing or additional testing. Extracts are stored at 4ºC. The laboratory management have established a procedure, S-178-n, for the Control of Clinical Material detailing the storage of these samples.

Hazardous substances:

There are separate cabinets for the storage of duty-free spirits, other flammable liquids, acids, alkalis and toxic chemicals. Non-toxic chemicals are stored in the appropriately labelled cupboard in the laboratory.

Reagents and consumables:

Reagents and controls are stored at 4ºC, -20ºC or -70ºC as required in fridges and freezers in the laboratory or storerooms.

Some reagents may be stored at room temperature. Consumables are stored in various locations within the laboratory and store rooms.

Temperature and humidity are monitored at appropriate room locations throughout the laboratory and in fridges and freezers in accordance with S-36-n.

Waste material for disposal:

This is stored in the laboratory in large, rigid, lidded containers prior to autoclaving. Autoclaved waste is transported to the clinical waste skip at the rear of the laboratory to be removed by authorised agents. The laboratory have established a procedure 'Waste disposal and disinfection' S-51-n for the disposal of clinical waste.

5.2.4 Staff facilities

Toilets, which are cleaned and maintained by the Venture Centre, can be found in the corridor 5m away from the unit. Shower facilities and additional toilets are available further along the corridor. Basic catering and dining facilities are provided within the unit.

Members of staff are provided with locking desk drawers for the storage of personal effects and protective clothing is stored in various locations within the laboratory. There are no requirements for overnight accommodation.

5.2.5 Patients

Patient samples are not taken at Micropathology Limited.

5.2.6 Facility maintenance and environmental conditions

Micropathology Ltd have a procedure S-1877-n that details Facility maintenance and environmental conditions. There is a designated Health & Safety Co-ordinator and Fire Officer. They are responsible for defining, implementing and maintaining the Health and Safety and Fire procedures and relevant standards within the company to ensure it is maintained in a functional and reliable condition.

Fire risk assessments are carried out according to the protocol provided in Fire risk assessment procedure (S-31-n).

A copy of the Laboratory Safety Manual (R-589-n) and Waste Disposal Policy (S-51-n) is provided for each new employee and further copies are available in the laboratory.

Personal protective equipment (gloves, lab coats, eye protection) is available for each employee and visitors.

The laboratory containment facilities conform to the requirements of the Advisory Committee on Dangerous Pathogens guidelines.

Room temperature and humidity are monitored on a daily basis in accordance with S-36-n and results recorded on the forms S-1269-n, S-1402-n, S-1569-n.

The laboratory is divided into specific areas allowing effective separation between the pre-amplification (clean) and post-amplification (sequencing) rooms to prevent sample contamination. Please refer to the laboratory floor plan as detailed in Appendix 1.

5.3 Laboratory equipment reagents and consumables

5.3.1 Equipment

5.3.1.1 General

The laboratory management have established a procedure, for the proper procurement and management of equipment required to fulfil the needs and requirements of users and the provision of the service. See S-186-n Procurement and management of equipment. Details of preventative maintenance, incident reporting and equipment records are detailed within this SOP.

5.3.1.2 Equipment acceptance testing

The laboratory management have established a procedure, for the acceptance testing and verification of equipment (See S-804-n) to demonstrate acceptability of equipment performance and 'fitness for purpose' upon installation.

5.3.1.3 Equipment instructions for use

All relevant instruction manuals are either uploaded to the electronic Quality Management System software, iPassport, or are stored on the shelves in the laboratory foyer. In both instances, manuals are subject to document control as detailed in the procedure 'Document control' S-1-n.

5.3.1.4 Equipment calibration and metological traceability

The laboratory management has a procedure for the calibration of equipment S-223-n (Equipment Calibration and traceability) and for determination of traceability, where required, of any equipment involved in the diagnostic process.

5.3.1.5 Equipment maintenance and repair

The laboratory management have established a programme of preventative maintenance in accordance with the procedure S-186-n, Procurement and management of equipment.

Where equipment has to be removed from the direct control of the laboratory for servicing, or repair, its performance is verified upon return before routine use, as detailed in the procedure Equipment verification - Repair / on loan S-1058-n.

All equipment, where required, should be decontaminated, prior to repair or preventative maintenance. A decontamination certificate should be completed by laboratory staff (Decontamination certificate for contractors R-1557-n).

5.3.1.6 Equipment adverse incident reporting

Adverse incidents and accidents are reported in accordance with the procedure S-186-n, Procurement and management of equipment.

5.3.1.7 Equipment records

The inventory of equipment is kept in the database: Asset register.mdb. Equipment details are also held on the QMS iPassport. The inventory of pipettes is kept in a database F:\UKAS ISO15189 2012\Equipment\Pipettes. The pipette calibration records can be found in the 'Pipette Calibration Records' file in the laboratory and the relevant year folders within F:\UKAS ISO15189 2012\Equipment\Pipettes.

Thermal cycler calibrations certificates are located in the F:\UKAS ISO15189 2012\Equipment\Thermocycler Validations folder. Additionally all certificates are also attached to the corresponding equipment on iPassport.

Equipment preventative maintenance visits are recorded on the QMS iPassport and in three equipment folders "Equipment - Service contracts", "Equipment - Calibration certificates" and "Equipment - Service reports" stored in the Quality Management System cupboard.

To ensure all equipment post calibration or service is fit for purpose, service reports and calibration certificates are reviewed and signed and dated as a statement of acceptability (As defined in the Procurement of Management of Equipment procedure S-186-n).

5.3.2 Reagents and consumables.

The laboratory management have established a procedure, for the proper management of all materials used in the provision of the service. See S-192-n Reagents and consumables (Management of materials) for details on reception and storage, acceptance testing, inventory management, instructions for use, adverse incident reporting and records. In-house databases are used to record primer and control batches and acceptance testing in accordance with the procedure S- 1696-n Online controls register user guide and S-1790-n Primer eregister user guide.

5.4 Pre-examination processes

5.4.2 Information for users

Details of the laboratory services including examinations, laboratory location and hours of operation, completion of the request form, transportation of samples, requirements for consent, sample rejection criteria and factors affecting the performance of examination or interpretation of results are detailed in the Laboratory User Handbook (S-748-n).

The laboratory produce a series of educational information sheets covering several tests offered by Micropathology Ltd. These are readily available on the company website www.micropathology.com for reference.

Micropathology Limited prefers to deal with healthcare providers and diagnostic laboratories, however some special interest groups of patients approach Prof. Fink directly. Investigative tests on samples from these patients will only be considered if Prof. Fink or a GP referral (to Prof. Colin Fink) are received.

Additionally, the laboratory receives requests from HM Coroners for identification of human remains. The company will NOT undertake receipt of specimens for testing directly from members of the public, for reasons of medical safety.

5.4.3 Request form information

The company accepts requests for diagnostic testing on any locally sourced pathology request form. The company will only carry out testing from *bona fide* laboratory, hospital or medical practitioner sources.

Users are able to source standard request forms and request forms for the identification of human remains via our website (http://www.micropathology.com/) . Alternatively users may contact the company directly. Requests for additional testing on a sample already received may be made by telephone, fax or email as detailed in the Laboratory User Handbook (S-748-n) and the procedure 'Additional test requests' S-809-n. .

Details for the completion of the request form are included in the Laboratory User Handbook (S-748-n).

5.4.4 Primary Sample Collection and Handling

5.4.4.1 General

Micropathology Limited mainly handles specimens that have been collected by our clients who are themselves familiar with the safety requirements necessary for their transportation. Specimens received by the laboratory are subject to handling conditions laid out in the Laboratory Safety Manual (R-589-n) and in the SOP S-10-n: (Specimen receipt (Accessions)). Sample volume requirements are stated in the User Handbook.

Details ensuring unequivocal link between the patient sample and the request form are provided in the Laboratory User handbook (S-748-n).

For the identification of human remains service, tissue samples are generally provided by hospital mortuary services. Personal items from the deceased or mouth swab specimens from close relatives are usually collected by police officers or coroner's assistants. Information on secure specimen collection is available from the laboratory.

5.4.4.2 Instructions for pre-collection activities

The laboratory provides instructions for the proper completion of request forms in the Laboratory user handbook S-748-n. Micropathology Limited are not involved in the collection of primary samples from patients. Samples requiring further preparation upon receipt into the laboratory are handled in accordance with the Specimen receipt procedure, S-10-n.

5.4.4.3 Instructions for collection acitivities

The laboratory are not involved in the collection of primary samples from patients.

5.4.5 Specimen Transportation

Transport of specimens to other diagnostic laboratories at the clients request, or return the sample to the sender, is performed according to the SOP 'Specimen transportation' (S-779-n). The correct packaging of samples for transportation is detailed in the Laboratory Safety Manual (R-589-n).

5.4.6 Specimen Reception

Specimen receipt is performed according to the SOP S-10-n, 'Specimen receipt (Accessions)'. Rejection of specimens is also covered in this SOP.

The date and time of receipt of samples into the laboratory is captured both in the LIMS system and additionally on an accessions sample labelling form (S-859-n). The identity of the persons receiving the sample into the laboratory is captured on the accessions sample labelling form (S-859-n).

Urgent samples are handled in accordance with the procedure S-10-n, 'Specimen receipt (Accessions)'.

5.4.7 Pre-examination handling, preparation and storage

Details of patient sample security, protection from deterioration, loss and damage are included in the procedure, S-178-n, for the Procedure for the Control of Clinical Material.

Time limits for requesting additional examinations are detailed in the Laboratory User Handbook (S-748-n).

5.5 Examination processes

5.5.1 Selection, verification and validation of examination procedures

5.5.1.1 General

The laboratory selects examination procedures, which have been validated, or verified using the procedures detailed below (5.5.1.2 and 5.5.1.3) for diagnostic use. The persons involved in testing diagnostic samples are recorded on laboratory worksheets (S-639-n, S-716-n, S-717-n, S-807-n, S-901-n, S-1137-n, S-1244-n, S-1245-n, S-1246-n, S-1247-n, S-1484-n), which are subsequently electronically archived, or are recorded on the equipment used in the analysis of the patient samples.

5.5.1.2 Verification of examination procedures

The laboratory has a procedure for the validation of examination procedures used without modification. Diagnostic kits used without modification, and equipment, are verified using the procedure 'Equipment / method verification of examination procedures' S-804-n through the examination of objective evidence and comparison to the manufacturers performance characteristics.

Completed verifications are subject to document control (S-1-n) and are held electronically on the QMS, iPassport.

5.5.1.3 Validation of examination procedures

In-house diagnostic assays, non-standard methods, standard methods used outside the intended scope or validated methods subsequently modified are all validated for their intended use prior to their introduction according the SOP Assay validation - MASTER (S-508-n) and template (S-266-n). Validation procedures for each assay are recorded using this template and include the objective evidence in the form of performance characteristics, in support of the assay validation.

Completed validations are subject to document control (S-1-n) and are held electronically on the QMS, iPassport.

The company is exempt from a requirement for CE marking of assays (European Union directive 98/79/EC for *in vitro* diagnostic medical devices) as it is designated a 'Health Institution' by the Department of Health.

When examination procedures are changed so that results or their interpretation may be significantly different then Micropathology Limited informs all users of the service by letter, fax or email in advance of the change and/or addition of a caveat to reported results informing clients of an impending or recent alteration.

5.5.1.4 Measurement uncertainty

The laboratory management have a document 'Uncertainty of measurement and Quality control monitoring' S-910-n which details the estimation of measurement uncertainty for assays and other 'imported uncertainties, which may influence the results of an assay.

5.5.2 Biological reference intervals or clinical decision values

Reference values for serology assays are detailed in the Laboratory User handbook, S-748-n.

The Laboratory management have two documents 'Master SOP' (S-5-n) and Assay validation –MASTER (S-508-n) that details the inclusion of biological reference intervals or clinical decision values where appropriate.

5.5.3 Documentation of examination procedures

Diagnostic assays are performed according to Standard Operating Procedures that are available on the QMS, iPassport. A template is provided for the guidance of those writing new procedures S-5-n (Master SOP).

Manufacturer's instructions are held electronically on iPassport as controlled (external) documents. Deviations from the instructions are validated, documented and reviewed separately.

All documents associated with the performance of the examinations are also subject to document control (S-1-n).

When examination procedures are changed so that results or their interpretation may be significantly different then Micropathology Limited informs all users of the service by letter, fax or email in advance of the change and/or addition of a caveat to reported results informing clients of an impending alteration.

5.6 Ensuring quality of examination procedures

5.6.1 General

Micropathology Ltd have a procedure S-1877-n that details Facility maintenance and environmental conditions. This details procedures the company undertakes to ensure that the quality of examination procedures is maintained.

In addition, the quality of examinations is ensured by the application of the following processes and procedures:

a) Internal Quality Control of ELISAs - S-158-n.
b) The inclusion of positive and negative controls in nucleic acid detection assays is detailed in the relevant SOPs and associated validation procedures.
c) Assay internal positive control is detailed in the SOP Ensuring the Quality of examination results – Repeat testing of samples S-796-n.
d) External Quality Assessment schemes – Participation in EQA schemes is detailed in the Inter-laboratory comparisons (EQA) S-531-n and Procedures for evaluation and improvement S-187-n SOPs.
e) Internal Quality Assurance - IQA S-183-n.

5.6.2.1 General

The laboratory uses quality control materials in all diagnostic assays in accordance with instructions detailed in assay specific assay validations / SOPs or manufacturers specifications.

5.6.2.2 Quality Control materials

The laboratory use Quality controls of diagnostic kits in accordance with manufacturers specifications. All kit instructions are held on the electronic Quality Management system iPassport in accordance with the procedure, Document control S-1-n.

All controls used in in-house validated assays are used in accordance with the assay specific SOP. They are used in a manner to mimic patient samples at or near to the limit of detection of the assay (Assay validation – MASTER S-508-n and Master SOP S-5-n).

5.6.2.3 Quality control data

The laboratory management has a procedure 'Ensuring the quality of examination procedures - repeat testing of samples' S-796-n which prevent the release of patient results in the event of quality control failure.

The laboratory have designed an excel based program which monitors the Quality controls of quantitative and qualitative assays to detect trends in examination performance that may indicate problems in the examination system (S-910-n Uncertainty of measurement and Quality Control Monitoring).

5.6.3 Inter-laboratory comparisons

5.6.3.1 Participation

The laboratory management have a document, Inter laboratory comparison (EQA) S-531-n, detailing the requirement for the laboratory to participate in suitable external quality assurance panels.

5.6.3.2 Alternative approaches

The procedure Inter laboratory comparison (EQA) S-531-n, also details , the requirement to arrange informal inter laboratory comparisons in the absence of a suitable formal external panel.

5.6.3.3 Analysis of interlaboratory comparison samples

The handling, processing and testing of inter-laboratory comparison samples is detailed in the Inter laboratory comparison (EQA) procedure S-531-n and the individual procedures for analysis of EQA panels from QCMD (S-1158-n), NEQAS (S-1558-n) and INSTAND (S-1534-n).

5.6.3.4 Evaluation of laboratory performance

The evaluation of laboratory performance in inter-laboratory comparison schemes is recorded on:

- EQA Analysis form (QCMD/NEQAS) S-1433-n
- Instand review form S-881-n
- NEQAS EQA review form S-570-n

in accordance with the procedure Inter laboratory comparison (EQA) procedure S-531-n and individual procedures for analysis of EQA panels from QCMD (S-1158-n), NEQAS (S-1558-n) and INSTAND (S-1534-n). Results are also discussed in various laboratory and / or Quality meetings, all of which are minuted and the minutes available on iPassport, the electronic Quality Management system.

5.6.4 Comparability of results

Staff consider the comparability of patient sample results, using different equipment and procedures, during the validation processes (Assay validation – MASTER S-508-n).

5.7 Post-examination processes

5.7.1 Review of results

Staff review results prior to release in accordance with the procedure ‘Results release’ S-1063-n. Consideration is paid to the performance of the quality control material, the patient clinical history and any relevant patient testing history.

5.7.2 Storage, retention and disposal of clinical samples

The laboratory management have a documented procedure S-178-n, for the control of clinical material, detailing the identification, collection, retention, indexing, access, storage, maintenance and safe disposal of clinical samples.

5.8 Reporting of results

5.8.1 General

All results are recorded and reported using StarLIMS in accordance with the SOP ‘StarLIMS Usage’ S-42-n. In accordance with the laboratory document, MASTER SOP template, each examination procedure should define the ‘Calculation of results’ and ‘Acceptance criteria’.

Reports are faxed or emailed to clients on the day that they are generated. This is detailed in the procedure ‘Results release’ S-1063-n.

Turnaround times are set by measurement of the median time between sample receipt and result availability. Weekends are not included in test turnaround time calculations. Batching is rarely applied to samples and when this happens the client’s needs and requirements are always considered. Users are informed by fax, email or telephone if results will be delayed by assay or equipment failure as detailed in ‘Results release’ S-1063-n.

5.8.2 Report attributes

Space is included on all Micropathology Ltd results reports produced by the LIMS for comments on sample quality, sample suitability, critical results and interpretative comments.

5.8.3 Report content

All reports transmitted from Micropathology Ltd include the examination performed, including those by a referral laboratory, the examination results, biological reference values / critical decision values, interpretation of results, any other comments particularly those concerning the points in report attributes.

The report issuing laboratory, patient identification, requesters identification, date of primary sample collection, type of primary sample, name of the person reviewing and authorising the results, date and time of report release and report pagination are also included.

5.9 Release of results

5.9.1 General

The laboratory management have established a procedure, S-1063-n Results release, detailing who may release results and to whom. This document also details the procedure to take when results fall within an 'alert' or 'critical' value and for those results given over the telephone. Records are maintained of any results given over the telephone, in particular with reference to a critical result on the telephone message logging form (S-808-n). These records are attached to the relevant patient entry in StarLIMS.
A final report always follows those results transmitted as an interim.

5.9.3 Automated selection and reporting of results

The laboratory does not automatically select and report results.

5.9.4 Revised reports

The laboratory management have established a procedure, S-1063-n Results release, for issuing an amended report. The original report remains with the relevant patient entry in StarLIMS.

5.10 Laboratory Information Management

5.10.1 General

The Employee contract (Employee handbook and statement of main terms and conditions) and 'Safety and Confidentiality Agreement' ensure the confidentiality of patient information by all staff upon commencement of employment at Micropathology Ltd. The Control of Records procedure, S-177-n, details the security in place at Micropathology Limited to prevent unauthorised access to all confidential patient and company records.

The company is also registered with the Information Commissioners Office for Data Protection.

5.10.2 Authorities and responsibilities

The authorities and responsibilities for the management of the information system are detailed in the documented procedure 'StarLIMS Usage' S-42-n.

5.10.3 Information system management

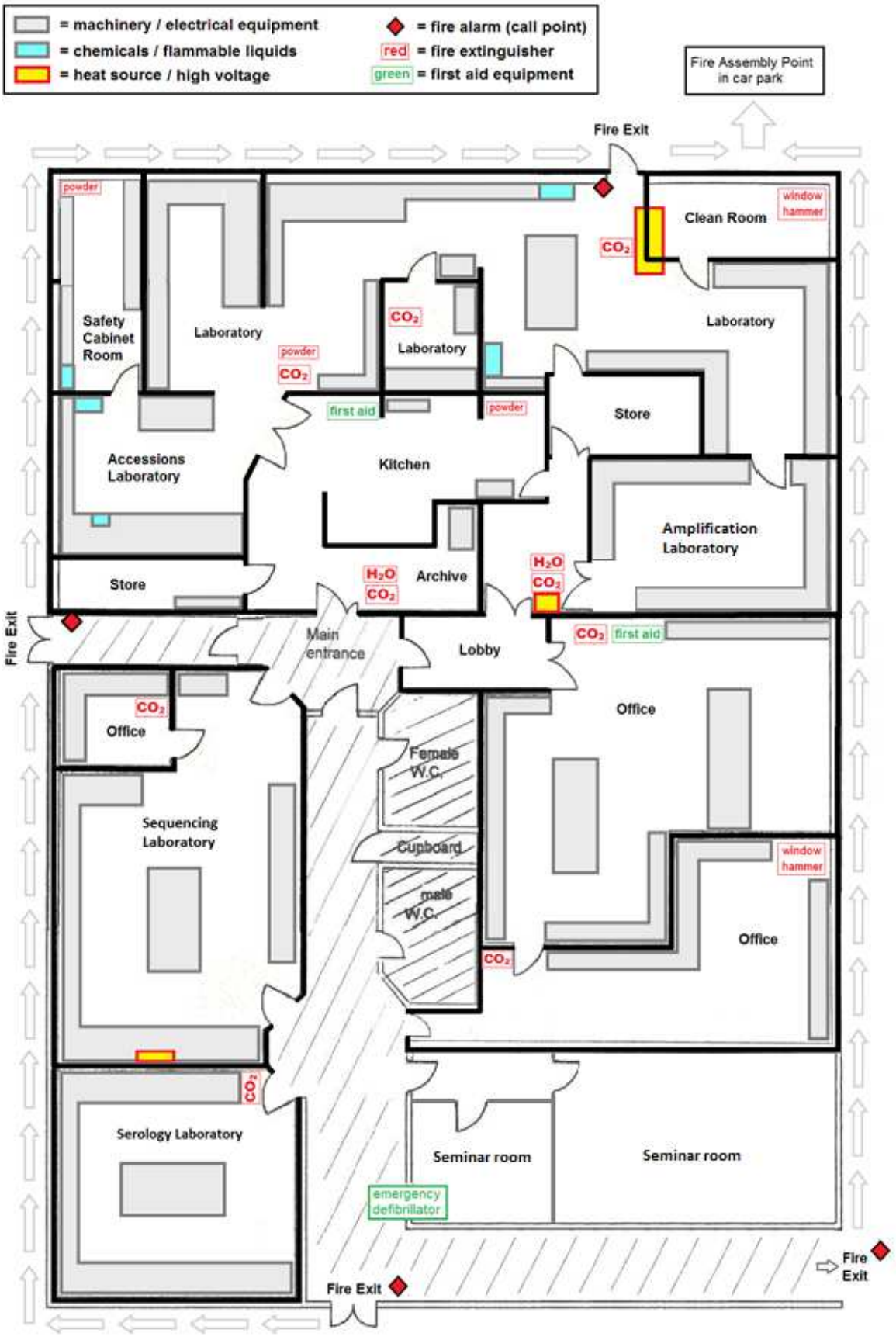
The laboratory management have a documented procedure ‘Software systems change procedure S-1833-n for managing changes prior and postimplementation. Micropathology Ltd. co-operate with clients to verify information systems, where appropriate.

The day to day functioning of the system is documented in the procedure ‘StarLIMS Usage’ S-42-n.

The laboratory management have a documented procedure ‘Contingency plan’ S-259-n, to maintain services in the event of failure or downtime in the information systems which affect the laboratory service.

The Control of Records procedure, S-177-n, details the security in place at Micropathology Limited to prevent records deterioration.

Appendix 1 – Floor Plan



Note: Shaded areas are not part of Micropathology Ltd.