The National Cancer Screening Service is part of the Health Service Executive. It encompasses BreastCheck – The National Breast Screening Programme and CervicalCheck – The National Cervical Screening Programme, BowelScreen – The National Bowel Screening Programme and Diabetic RetinaScreen – The National Diabetic Retinal Screening Programme.
Chapter 7
Quality assurance in histopathology

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7.3 References
7.1 Introduction

Cervical cytology currently represents the primary screening method. Colposcopy locates the most abnormal areas of the cervix. Histopathology provides the final diagnosis of cervical neoplasia, forming the basis for which treatment is planned.

In addition, histopathology:

- Serves as the ‘gold standard’ for quality control of cytology and colposcopy
- Is the source of diagnostic data stored at the National Cancer Registry Ireland (NCRI) and used for evaluation of screening programmes
- Is required to diagnose the degree of abnormality in women with persistent low grade abnormalities including HPV lesions, as well as high grade lesions (squamous and glandular)
- May also diagnose either glandular abnormalities or high grade CIN, adenocarcinoma-in-situ (AIS), or invasive cancer.

As in cytopathology, the sample pathway for histopathology can be subdivided into three key stages:

1. Sample taking, sample transport and receipt of sample in the laboratory (pre-analytical)

   The accuracy of the histopathological diagnosis of tissue specimens depends on adequate quality samples, obtained by colposcopically directed punch biopsies (with endocervical curettage, if necessary) or excision of the Transformation Zone (TZ) or conisation.

2. Sample processing and interpretation (analytical)

   Accurate histopathological diagnosis further depends on appropriate macroscopic description, technical processing, microscopic interpretation and quality management correlating cytological and histological diagnosis.

3. Report generation (post-analytical)

   It is important to recognise that the interpretative reports provided in histopathology and cytopathology are the opinion of the reporting pathologists. There is therefore a subjective element in the content of any report. Some diagnoses require the combined input of a colposcopist, cytologist and histopathologist. There are a variety of reasons why clinical appearances, cytology, biopsy and excision results may appear discrepant. Multi-disciplinary team (MDT) meetings can often resolve perceived discrepancies. If a colposcopist is unsure of the significance or meaning of a report or feels that a report is incorrect, they should contact the issuing laboratory or reporting pathologist. Histopathologists should remain abreast of current and emerging interpretation guidelines\(^1,2,3\).

The quality requirements and standards for histopathology laboratories providing services to CervicalCheck are set with regard to:

- NCSS Guidelines for Quality Assurance in Cervical Screening (first edition)
- ‘Guidelines for the Implementation of a National Quality Assurance Programme in Histopathology - Faculty of Pathology, Royal College of Physicians in Ireland’\(^1\)
- Standards and guidelines, revised in response to technological developments and research outcomes, in other cervical screening programmes, with particular reference to histopathology reporting (NHS CSP\(^2\), Royal College of Pathology\(^3\))
- The activity and performance metrics for histopathology collated since the commencement of CervicalCheck.
Compliance with the requirements and standards is measured and monitored by:

- Quality metrics reports by histopathology laboratories
- Analysis of data provided to the Cervical Screening Register (CSR) by cytopathology, colposcopy and histology service providers
- Quality assurance site visits to laboratory service providers
- Monitoring and review of operational activity and performance.

7.2 Quality requirements and standards

Ensuring quality assurance in service delivery comprises compliance with both quality requirements and quality standards.

Quality requirements are stated as a description. There are no targets associated with a requirement as service providers must fulfil the requirement.

Quality standards are stated as a description of an activity with a measurable level of performance, with an associated target for achievement. The standards are designed to be measurable i.e. quantitative with criteria that are valid, reliable and feasible.

7.2.1 Organisational requirements

**Standard 7-1 Accreditation**

The laboratory must have and maintain accreditation to ISO15189 standard or equivalent, certified and documented by an approved accreditation body. The scope of the laboratory accreditation must include histopathology.

External accreditation at least once every 2 years.

*Note: Laboratory accreditation covers facilities, staff qualifications, training and competencies, equipment, laboratory information systems, and quality management systems.*

**Data protection**

All data protection issues (storage, access, security, confidentiality and data transfer) will be compliant with Irish and European legislative instruments: the Data Protection Act 1988, the Data Protection (Amendment) Act 2003 and any future revisions or amendments of the Act as well as the EU Directive 95/46/EC - The Data Protection Directive.

Laboratories must have facilities, systems and procedures to ensure the secure exchange of personal health information and confidential data. These provisions must apply equally to data held in paper and in computer formats. A Virtual Private Network (VPN) must be installed between the laboratory or hospital and the programme operations office for the secure exchange of electronic data.
Health and safety compliance
The laboratory will be compliant with all national legal and statutory health and safety requirements.

Quality management system (QMS)
The laboratory will have a quality management system (QMS) in place as required by their accreditation standard. The laboratory should have a designated person responsible for quality management who will liaise with CervicalCheck to resolve any quality issues that may arise.

Any complaints in relation to the histopathology service within the screening programme will be notified to CervicalCheck.

Laboratory information management system (LIMS)
- **General:** An appropriate laboratory information management system (LIMS) will be installed and be in operation in the laboratory. The LIMS will be in a secure facility with the provision for adequate back-up arrangements. Access to the LIMS will be by privilege-level access control. The LIMS will be capable of generating periodic quality metrics and audit returns to the NCSS. Ideally, there should be an electronic linkage to CervicalCheck to ensure prompt retrieval of results.
- **Data capture:** The LIMS will be capable of recording the minimum dataset from the sample and request form.
- **Reporting:** The LIMS will be capable of recording test results including the identity of the reporting pathologist(s). The LIMS will be capable of recording and storing SNOMED codes for results.
- In addition the laboratory information system will:
  - Link multiple test results for the same patient
  - Provide easy access to details about previous cervical histology of the patient
  - Provide the data necessary for evaluation of the CervicalCheck programme.

Changes to service capacity, capability or conformance to quality assurance (QA) standards
Any changes that have or could have an impact on any aspect of the laboratory services, including laboratory accreditation status, processes, system procedures, analysis, and reporting should be advised in advance to CervicalCheck.

Health agencies and authorities
Laboratories will comply with all requests for data or reports by Irish health agencies and authorities, including the Department of Health and the National Cancer Registry Ireland (NCRI).
7.2.2 Laboratory facilities

All laboratories will provide appropriate facilities. These will include appropriate areas for sample reception, cut-up, processing, reporting, typing and authorisation.

7.2.3 Staff qualifications

Scientific, medical and non-medical staff will be qualified for the positions they hold according to national requirements to practice. All equipment will be maintained and used only by laboratory staff that are competent to carry out such tasks.

The histopathology laboratory will be led by a medically qualified consultant who works in that discipline on a regular basis. All samples will be reported by a medically qualified consultant.

There will be a lead medical scientist who is responsible for the day-to-day management of the department and who has responsibility for supervision of non-medical staff.

7.2.4 Specimen reception

Standard operating procedures (SOPs) will be in place for handling CervicalCheck samples.

For the purposes of data capture, samples originating from CervicalCheck colposcopy services must be segregated from samples from other sources. This may be via the programme’s Cervical Histology Form (where applicable) or by an accredited laboratory form where the origin of a sample is clearly identifiable. The issue of consent by the woman should be incorporated into the processes for sample data capture and data exchange.

All cervical histology forms will be date-stamped upon receipt.

All histopathological specimens must be received in either 10 per cent buffered formalin or as fresh samples and in an appropriate specimen container.

Sample containers will be matched to forms prior to labelling. Cross-checking of a minimum of three patient identifiers will be performed to ensure correct identification.

A discrepancy handling and resolution process will be in place to manage all discrepancies with CervicalCheck samples received.

After verification of correct correlation of the sample vial with the corresponding Cervical Histology Form, and acceptance of the sample and form for processing, both will be labeled with a unique identification number which is generated by the LIMS. The sample will be labeled on the top and side of the specimen container.

7.2.5 Data entry and notification to CervicalCheck

Relevant clinical details recorded on the Cervical Histology Form will be recorded. Notification and result files should be sent to CervicalCheck on a regular basis. A periodic reconciliation of files sent and received should be in place between CervicalCheck and the laboratory.
7.2.6 Assessment of the sample (cut-up)

The cut-up of the histopathological specimens will be performed either by a laboratory scientist, pathologist or anatomic pathology technician. The RCPath Dataset for Histological Reporting of Cervical Neoplasia can be used to guide cut-up procedures.

Specimen description and sampling will be done in such a way as to facilitate microscopic reporting (and pathological staging). As margin involvement may be associated with persistent or recurrent disease, every effort will be made to identify whether margins are involved or are free of disease.

Laboratories may use different means (including inking, where required) when assessing margins.

**Quality requirement**

**Sample ‘chain of custody’**

Handling procedures will ensure a robust ‘chain of custody’ across the specimen pathway. These involve the cross-checking of a minimum of three patient identifiers at each stage, to typically include name, hospital number and accession number.

Slide labels will include patient surname in addition to the accession number.

**Cervical biopsy (not otherwise specified), wedge biopsy and cervical punch biopsy**

Careful handling of specimens is recommended to prevent surface trauma and disruption or loss of surface epithelium.

All tissue will be embedded in such a way as to minimise any loss of tissue during processing. Macroscopic description should include measurements and number of fragments.

**Endocervical curettage**

The aggregated size (in three dimensions) of the sample is recorded. All tissue will be embedded in such a way as to minimise any loss of tissue during processing.

**Cervical cone biopsy and cervical loop biopsy/large loop excision of the Transformation Zone (LLETZ), needle excision of the Transformation Zone (NETZ), straight wire excision of the Transformation Zone (SWETZ) and Cone**

Macroscopic description should include measurements in three dimensions. Care may be needed to ensure that the correct cut face is placed face down in the cassette.

These specimens will be blocked in their entirety. Cassettes will be separately identified, with a block designation to indicate their origin, if required.
Trachelectomy
Macroscopic description will include measurements in three dimensions. Bearing in mind that margin involvement will influence further treatment, sampling will be directed in such a way as to identify the final surgical margin on microscopy (where possible). Inking may be considered.

In radical trachelectomy, the vaginal and parametrial margin should be sampled in such a way as to allow a microscopic description of differential margin status.

Lymph nodes
Where submitted, a gross description will take place with any pertinent macroscopic description. All identified lymph nodes will be submitted for microscopic examination.

Uterus
Macroscopic description including measurements in three dimensions will be entered into the LIMS (via electronic or manual dictation system).

The resection margins will be identified appropriately (e.g. vaginal, radial resection margin of cervix, parametrium etc.).

Macroscopic description will include a description of any lesion (with measurement).

In the case of radical hysterectomy, any resected lymph nodes must be described, measured and counted (and designated according to the anatomical site from which they have been removed).

Specimen dissection and block selection will be carried out in accordance with an agreed standard. Templates exist to guide specimen dissection and sampling and can be used where necessary e.g. the RCPath Dataset for Histological Reporting of Cervical Neoplasia (3rd edition) April 2011.

7.2.7 Sample processing
Appropriate and standardised procedures will be in place for specimen processing. Quality management systems will surround these procedures.

7.2.8 Sample embedding
Dedicated facilities will be provided for sample embedding and a record will be kept of any tissue that does not survive the tissue processing schedule.
7.2.9 Sample sectioning

Appropriate procedures will be in place for sample sectioning. Health and safety procedures will be followed at all times to prevent cuts from microtome blades.

**Quality requirement**

- Cervical biopsy (not otherwise specified) and cervical punch biopsy
  
  In general, it is recommended that three levels of such biopsies are cut.

- Cervical cone biopsy and cervical loop biopsy/large loop excision of the transformation zone (LLETZ), needle excision of the transformation zone (NETZ), straight wire excision of the transformation zone (SWETZ) and Cone/cervical wedge biopsy/endocervical curettage (ECC)/uterus
  
  A single level from each block may be likely to suffice initially, but further levels may be required by the pathologist.

7.2.10 Slide staining

Appropriate procedures should be in place for slide staining. Typically this will be Haematoxylin and Eosin. Special stains and immunohistochemical stains will be employed as required by the pathologist. Stains, reagents and protocols will be prepared and used according to manufacturer’s instructions with appropriate regard to both positive and negative control slides.

Internal technical quality assurance checks will be carried out routinely including quality of staining and quality of preparation.

7.2.11 Proficiency and competency of staff

**Quality requirement**

- **All staff**
  
  All staff will be competent to carry out their roles. Competency will be maintained by regular training and education. Training and competency records should be retained and available for review.

- **Pathologists**
  
  All pathologists will participate in continuing medical education (CME) as required by Part 11 of the Medical Practitioners Act 2007 – Maintenance of Professional Competence. 
Lead medical scientist, manager, supervisory scientific staff

The lead medical scientist will be responsible for maintaining a high quality service. Sufficient supervisory scientific staff will be available to provide satisfactory supervision for the training, service development and quality control of staff.

Internal quality control

Microscopic diagnosis is crucially dependant on quality control.

Methods used for quality assessment will incorporate a process of continuous dialogue within the laboratory and improve individual histopathology reporting accuracy.

Internal quality control of reporting can be monitored by a variety of methods and could include:

- Performance evaluations
- Periodic audit of histopathology outcomes
- Monitoring of non-conformities
- MDT review of slides
- Monitoring histopathology detection and reporting rates
- Correlation of cytology with clinical/histological outcome.

Pathologists will participate in regular clinico-pathological conferences (CPC)/multi-disciplinary team (MDT) meetings\(^\text{10}\).

Continuing education

Continuing education will be facilitated with evidence of internal and external educational activities.

7.2.12 Microscopy and reporting of results

The reporting of the histopathological specimens will be performed by a pathologist. The relevant RCPath Dataset (currently Histological Reporting of Cervical Neoplasia (3rd edition))\(^\text{11}\) can be used as a reporting guide.

All histopathology reports must be authorised by a consultant pathologist (electronic and/or manual).

All histopathological results must be entered onto a computerised system (laboratory information management system [LIMS]) to allow quality assessment. Amended reports and supplementary reports will be auditable.

Reports will record the origin of the specimen, identify the tissue components that are present, provide a macroscopic description and microscopic diagnosis along with the identity of the reporting pathologist.
The microscopic diagnosis will record all grades of squamous and/or glandular intra-epithelial neoplasia, and invasive lesions.

The distribution of a lesion will note if an orientated specimen has been submitted. Any invasive lesions are classified and graded according to national protocols and guidelines.

Where an excision procedure has been undertaken, any microscopic report will attempt to indicate whether or not the squamous or glandular lesion has been completely excised.

In the case of radical trachelectomy, this will include the vaginal and parametrial margins. In the case of radical hysterectomy, the report will contain specific comment on resected lymph nodes, including site designation, number (in total) and number involved by tumour (if applicable).

Features that impair interpretation will be recorded.

Other significant pathologic features, such as significant inflammatory changes will be recorded.

When a biopsy fails to reveal the source of the abnormal cells in a smear test, it is important to differentiate between a biopsy that is technically adequate but fails to identify a lesion, and a biopsy that is technically inadequate.

All reports will be coded (typically using standardised SNOMED nomenclature) to allow data collection.

### Authorisation of results

Every result will be appropriately authorised before release. Every report should be checked for inconsistencies before authorisation.

### Recording of results

Results details will include at least:

- Patient identification data
- Name and address of the laboratory
- Name of requesting physician
- Laboratory ID number
- Date of specimen procurement (specimen date)
- Date of arrival of the specimen in the laboratory
- Sample type
- Anatomical site of origin
- Relevant clinical details
- The results of the laboratory examination in accordance with the current standard classification system and data format, including a judgment of the quality and adequacy of the histopathological slide (if necessary), date of authorisation of the final report, and name of pathologist who has evaluated the sample.
Standard 7-2

**Turnaround time (TAT):**

Time between date of reporting results of the specimen from date of specimen arrival within the laboratory.

- Small specimens
  > 90% within 4 weeks of the woman’s attendance
  At least 80% within 10 days.

- Large specimens
  At least 80% within 14 days.

*Note:* Biopsies are performed on small specimens (<3 blocks). LLETZ, cone, trachelectomy, hysterectomy are performed on large specimens.

Standard 7-3

**Results reports**

Results, once authorised and released, must be issued promptly to the ordering doctor or clinic.

100% to be received within 5 days of report being authorised.

Delivery of results reports to ordering doctors or clinics

Results reports will be issued to the correct ordering doctor or clinic. The laboratory will ensure that an appropriate delivery mechanism (for reports) is in place.

Review requests and amended reports

Laboratories will have procedures in place to manage and respond to requests for second opinions and to issue amended or addendum reports as necessary. Additional or amended reports, once authorised and released, must adhere to the same standards and targets.
### 7.2.13 Archiving

Administration, archiving and disposal procedures will comply with accreditation standards and national and regional legislation, including that relating to confidentiality and data security of personal health information and disposal of hazardous medical waste or chemicals.

#### Standard 7-4

<table>
<thead>
<tr>
<th>Storage and archiving</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Secure archiving of cervical histology forms, blocks, slides and written and/or computerised reports is required for specific retention periods.</td>
<td>100% to be received within 5 days of report being authorised.</td>
</tr>
<tr>
<td>Cervical histology forms or their electronic equivalent</td>
<td>Specimens Blocks, Slides, Reports</td>
</tr>
<tr>
<td>Until authorisation.</td>
<td>Until authorisation.</td>
</tr>
<tr>
<td>30 years</td>
<td></td>
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</table>

**Note 1:** Cervical histology forms may be in paper format or in their electronic equivalent, as per local accredited practice.

**Note 2:** All slides/blocks will be stored in conditions adequate for preservation.

**Note 3:** Records will be stored to allow prompt retrieval if required.

#### Quality requirement

**Specimens retained and for disposal**

Logs of specimens retained and for disposal will be maintained. Samples will not be disposed of prior to final report authorisation by the pathologist. Retention of specimens will comply with relevant legislation.

#### Quality requirement

**Access to materials**

Laboratories are required to provide CervicalCheck access to materials including slides and records on request.
7.2.14 Clinico-pathological conferences (CPC)/multi-disciplinary team (MDT) meetings

There are a wide variety of reasons for cases to be included in CPC/MDT meetings\(^\text{10}\). Cases discussed may include perceived discrepancies between cytology, histology and clinical appearances.

### Participation in CPC/MDT meetings

Histopathologists (with or without other scientific staff members) are integral participants in CPC/MDT meetings\(^\text{10}\).

CPC/MDT meetings are convened by and organised by programme colposcopy services. The locations, timing and frequency of CPC/MDT meetings may vary from time to time but reasonable notice will be provided by the colposcopy service to the laboratory. While clinical teams are primarily responsible for case selection, laboratories are encouraged to submit cases for discussion. CPC/MDT meetings and cases require preparation.

### Protocol for CPC/MDT meetings

Participation, including a signed record of personnel attending and operational decisions, will be recorded by a person nominated by the programme. Participants must be subject to confidentiality and data protection requirements\(^\text{5,6,10}\).

Laboratories are encouraged to incorporate CPC/MDT meetings into the internal continuing education of scientific staff within the laboratory.

### Case selection

To ensure the efficient running of CPC/MDT meetings, cases will be appropriately selected by the colposcopist responsible for the patient. Clinicians should be aware of any relevant clinical history and should have a clear understanding about the reason for CPC/MDT discussion.
7.2.15 CervicalCheck cancer review process

The CervicalCheck Cancer Review Process reviews notified cases of invasive cervical cancers. It operates as a feedback and learning process within quality assurance, contributing to potential continuous improvement measures. This may lead to a request from CervicalCheck for any diagnostic material to be reviewed internally or externally.

**Quality requirement**

Review of histology slides

The laboratory will review slides for women with a diagnosis of invasive cancer where such is requested by the programme or treating clinician and issue the results of these reviews to the programme.

**Quality requirement**

Independent third-party review

Laboratories will provide all case material where requested for cases identified as warranting independent third-party review by the process for cervical cancer review.

7.2.16 Quality assurance and continuous improvement

**Quality requirement**

External quality assurance (EQA)

Laboratories will participate, and show adequate performance, in accredited external quality assurance (EQA) schemes for histopathology and for technical quality.

**Standard 7-5**

Quality metrics

A complete and accurate report containing prescribed quality metrics will be provided at regular intervals to CervicalCheck.

Complete data at least quarterly, to be received by CervicalCheck within 1 month of quarter-end.
The quality metrics collected during internal quality control procedures are used to:

- Continuously analyse performance
- Spot trends and variations
- Complete annual returns
- Cross-reference data from multiple sources
- Produce rapid analysis
- Improve performance.

The quality metrics required are detailed in the current version of the CervicalCheck ‘Histo 1 Report’. They include measures which should be readily available from the laboratories internal quality control processes and are based on the QA metrics specified in the Faculty of Pathology Guidelines for the Implementation of a National Quality Assurance Programme in Histopathology.

The quality metrics include, among others, details of:

- Workload
- Consultations
- Correlation of frozen section diagnosis with final diagnosis (if service requested)
- Cytological/histological correlation and follow-up (where available)
- Retrospective review
- CPC/MDT meetings
- External quality assurance (EQA)
- Turnaround times (TATs).

Laboratories will have the ability to separate CervicalCheck workload from other workload(s) for statistical and monitoring purposes.

The identifier assigned to an individual pathologist will be the same for different sections of the report and over successive reporting periods.

### Quality metrics improvement

Laboratories will undertake appropriate and timely measures to address performance issues that impact on quality metrics and resulting values outside of laboratory, national and/or international norms.

Individuals identified as poorly performing may be required to be removed from working on CervicalCheck specimens until evidence exists that their proficiency in reporting is back in line. Evidence of retraining may be sought by the NCSS.

### Quality assurance visits

Laboratories will accommodate on-site visits by NCSS-designated personnel for quality monitoring, audit and assurance purposes, providing access to personnel, resources, processes, documentation and results.
7.3 References

1. Faculty of Pathology, Royal College of Physicians in Ireland (July 2011). Guidelines for the implementation of a National Quality Assurance Programme in Histopathology – Version 5.0.


8. CervicalCheck Cervical Histology Form (CS/F/LAB-1 Rev 3).


10. CervicalCheck Guidance for CPC/MDT meetings for colposcopy services - planning successful collaboration for web-based interactive meetings between colposcopy, histopathology and cytology.


13. Process for the review of incident cases of cervical cancer following the introduction of a national cervical screening programme (CS/PUB/PM-10).

The National Cancer Screening Service is part of the Health Service Executive. It encompasses BreastCheck – The National Breast Screening Programme and CervicalCheck – The National Cervical Screening Programme, BowelScreen – The National Bowel Screening Programme and Diabetic RetinaScreen – The National Diabetic Retinal Screening Programme.