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Technical requirements specific to molecular-genetic tests (Part 2)

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1 Information management

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What is INFORMATION ?

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Information includes

- patient information
- examination data
- quality control data
- management information
- procedures
- records

Information type

- computerized information
- non-computerized information
- undocumented information

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Confidentiality and Security

Laboratories shall have policies and procedures to:

- inform authorities and specify responsibilities for information management
- safeguard the patient's privacy
- ensure the confidentiality of laboratory data

Paper-based systems

- use durable materials for recording
- store information properly

Computerized systems

- schedule regular backups of data

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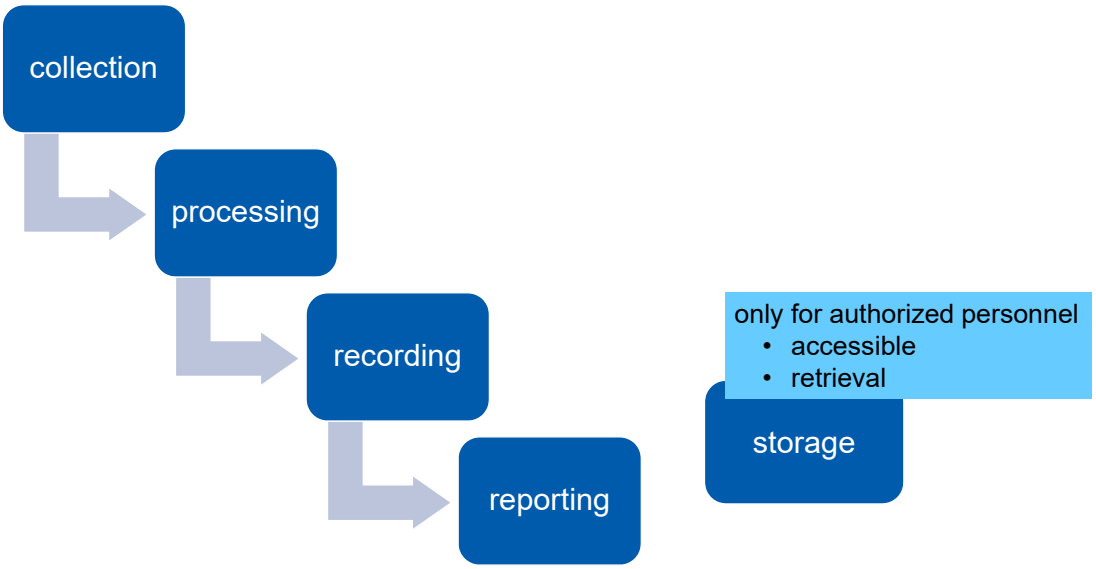
Information Control Process



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Computerized Systems

Software options

- systems developed in-house using commercial database software
- fully developed commercial systems

Computer system selection

- permanence, computer system maintenance, backups
- security, access confidentiality
- traceability
- system speed
- flexibility

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Computerized System Validation/Verification

Software and hardware shall be

- validated by the supplier and/or laboratory
- verified to confirm its function before implementation, with any change to the software
- retained validation and/or verification authorized records
- equipped with an interface

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Computerized System Management

Secured information within the computer system shall be

- protected from unauthorized access
- protected using cybersecurity measures
- protected against tampering or loss
- maintained in a manner that ensures the integrity of the data
- documented a contingency plan

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Interfaces and Off-Site Storage

Laboratories shall

- follow national or international data protection requirements
- ensure the integrity of information transferred through interfaces
- ensure that the off-site storage system complies with all requirements

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Information Management: Molecular Pathology

Referral examination

Next-generation sequencing (NGS) data transfer

- policy and procedure
- robust security

Genetic testing

- onset
- non-onset carrier diagnosis, presymptomatic diagnosis, prenatal diagnosis

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2 Documentation of examination procedures

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General Requirements for Document Control

- authorized personnel shall review and approve all documents before issue
- all documents shall be identified uniquely
  - title
  - identifier on every page
  - version and/or date of current edition
  - page number/total number of pages
  - authorized person for issue
- documents shall be legible and in a commonly understood language
- the current edition and distribution of the documents shall be listed
- contingencies shall be in place to track the changes in the revised document
- all documents shall be periodically reviewed by authorized personnel
- all obsolete documents shall be identified as such, and at least one obsolete document shall be retained for a specific time
- quick references shall be acceptable when a full documented procedure is provided

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Examination Procedure Documentation

Documents pertaining to examination procedures shall include the following, when applicable:

1. purpose of the examination
2. principle and method of the procedure used for examinations
3. performance characteristics
4. type of sample (e.g. plasma, serum, urine, tissue)
5. patient preparation
6. type of container and additives
7. required equipment and reagents
8. environmental and safety controls
9. calibration procedures (metrological traceability)
10. procedural steps
11. quality control procedures
12. interferences (e.g. lipaemia, haemolysis, bilirubinemia, drugs) and cross reactions
13. principle of procedure for calculating results including, where relevant, the measurement uncertainty of measured quantity values
14. biological reference intervals or clinical decision values
15. reportable interval of examination results
16. instructions for determining quantitative results when a result is not within the measurement interval
17. alert/critical values, where appropriate
18. laboratory clinical interpretation
19. potential sources of variation
20. references

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Examination Procedure for Molecular Testing; NGS

Upgrade monitoring

- instruments, sequencing chemistries, and reagents or kits used to generate NGS data

Benchtop NGS procedures

- DNA/RNA preparation for different types of samples, fragmentation, library preparation, barcoding (molecular indexing), sample pooling, and sequence generation

NGS bioinformatic pipeline

- all algorithms, software, and databases (referred to as components) used in the analysis, interpretation, and reporting of NGS results

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3 General personnel requirements

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Personnel Requirements

1. Qualification
2. Job descriptions
3. Orientation for new staff
4. Training
5. Continuing education
6. Competence evaluation
7. Staff performance review
8. Record

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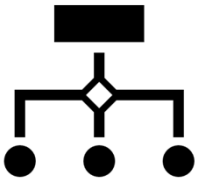
Qualifications and Job Descriptions (Points 1 and 2)

Personnel qualification for each position

such as Laboratory Director, Technical Supervisor, Clinical Consultant, General Supervisor, Manager, and Technical Personnel

Job descriptions for all personnel



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3. Orientation of New Staff

Orientation contents include but are not to be limited to

- organization
- work area's department
- employment terms and conditions
- facilities
- safety requirements
- occupational health services

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4. Training and Continuing Education

Essential training

- management system
- processes and procedures assigned as tasks
- information control with confidentially
- health and safety, including infection control, occupational health, and adverse incident and accident
- ethics

Supervision of undertrained personnel

Continuing education

periodic review of the effectiveness of training and the continuing education program

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Competence Evaluation and Staff Performance Review (Points 5 and 6)

Competence evaluation

- after training
- periodically
- managerial and technical tasks
- re-training, when needed

Staff performance review

- performance review after technical competence evaluation
- consideration of individual needs
- encouragement of productive work environments

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7. Records

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Personnel records shall be maintained on at least the following:

- educational and professional qualifications
- copy of certification or license to practice, when applicable
- previous work experience e.g., CV
- job descriptions
- orientation of new staff to the laboratory environment
- training in the current job tasks
- competency evaluation
- records of continuing education
- reviews of staff performance
- reports of accidents and exposure to occupational hazards
- immunization status, as relevant to the assigned duties

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4 Performance monitoring

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General

- ensure the quality of examinations
- appropriate pre- through post-examination processes
- internal quality control programs
- external quality control programs (see section 5)
- comparability of examination results

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Internal Quality Control Program; General-1

Quality control rule

- define the frequency of processing
- define the acceptable criteria
- revisions to the acceptance criteria

Quality control material

- react in a manner similar to patient samples

Non-control material

- moving average
- alternate procedure validated to ensure its metrological traceability
- retesting of patient samples
- use of reference materials

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Internal Quality Control Program; General-2

Quality control data

- evaluation and monitoring before releasing patient results
  - take corrective actions
  - review the results after the last successful quality control event
- monitor and review quality data periodically to detect trends
  - take preventive actions

Comparability of examination results

different procedures, equipment or methods

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Internal Quality Control Program; NGS-1

Wet Bench processes

- depth of coverage
- uniformity of coverage
- GC bias
- transition/transversion ratio (Ti/Tv ratio)
- base call quality scores
- mapping quality
- duplicate read success rate and removal of duplicate reads
- first-base read success
- decline in signal intensity
- strand bias

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Internal Quality Control Program; NGS-2

Bioinformatics pipelines

- deviation during analysis
- regular monitoring with proper quality control materials
- establishment of quality control metrics for NGS process components; DNA extraction, library preparation, DNA sequencing, and informatics analysis pipelines

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Internal Quality Control Program; Amplification

Nucleic acid amplification test

- monitor for cross-contamination
  - negative control
- to ensure the nucleic acid amplification reaction; for example, by using an internal control
  - internal control
- for qualitative tests, use negative and positive controls
- for quantitative tests, use a negative control and at least two positive controls

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5 External quality assessment and alternative method

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Participation

Responsibilities

- establish a process for EQA participation
- EQA program selection
  - fulfil ISO/IEC 17043
- instructions for participation
- definition of acceptable criteria
- corrective action taken when necessary

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Rule of EQA

Laboratories shall

- handle the EQA samples
- analyze the EQA samples and subject the EQA samples to treatments similar to those used for patient samples
- monitor and maintain records
- investigate deficiencies
- manage corrective actions
- communicate outcomes

Laboratories shall NOT

- hold discussions between laboratories
- refer to the samples for confirmation

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Alternative Method

Develop other approaches when EQA participations are not available

- policies and procedures
- records
- corrective/preventive action

Examples of alternative methods for molecular testing

- parallel sample testing in other laboratories
- repeating tests of samples
- conducting tests using different independent methods
- comparison with other parameters
- direct observation
- clinical correlation studies
- participation for multiple proficiency testing

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6 Post-examination

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General

Result reporting

- review of the results
- reporting of the results
  - accurately, clearly, and unambiguously
  - using internationally accepted vocabulary and nomenclature and appropriate language for the intended recipients
- release of the results to only the persons authorized

Post-examination handling of the samples

- handling procedure
- retention period
- disposal

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Report Content-1

Common requirements

- examinations performed
- name of the laboratory issuing the report
- location of performance of the laboratory examinations
- unique patient identification
- name or other unique identifier of the user and contact details
- date of primary sample collection and sample receipt
- type of primary sample and any specific information necessary to describe the sample
- measurement or examination procedure, where relevant
- reference intervals, clinical decision limits
- interpretation of results, where appropriate
- identification of the examinations undertaken as part of a research or development program
- date of the report and time of release
- identification of any results that need to be considered as preliminary

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Report Content-2

Specific requirements for reports

- comments on sample quality and suitability
- indications of critical results
- interpretive comments
- interpretation of results

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Report Content; Molecular Pathology

Reporting of secondary findings

- policy for reporting
  - not to report
  - ethical considerations

Information for interpretation

Additional information

- need for genetic counseling
- potential impact on family
- necessary additional testing

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Amendments to Results and Reports

Amended or revised results procedure shall be included

- clearly identified any change of information
- recognized by user the amendment or revision
- the date and time of the revision
- the name of the person responsible
- the original report entries remain in the record when revisions are made

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