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Quality management in cytogenetic laboratory

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The quality management (QM) program should incorporate the following elements:

- Goals and objectives
- A design to monitor, evaluate, and correct quality problems
- The monitoring of complaints and incidents
- The monitoring of all aspects of the laboratory's scope of care
- Addressing problems that interfere with patient care
- Describing procedures for collection and communication of quality and safety information (quality control (QC) and quality assurance (QA))
- Key quality indicators of laboratory operations that target quality improvements (QI) measures, such as test turnaround time, specimen acceptability, and test result accuracy
- Evidence of a regular review by the laboratory director or designee

The QM program includes the following areas: QC; individualized QC plan (IQCP); standards of test records and reporting; general culturing issues; QI; proficiency testing (PT); inspection preparation; calibration verification.

Quality issues in cytogenetic assays include: internal and external QC; laboratory accreditation; success rates; reporting of results; reporting times; introduction of new laboratory procedures; specimen handling; analysis interpretation; equipments; staffing; workload recommendation; storage and retention of specimens and documents.

1. QC program

The QC program supports functions in the following areas: Test standards and controls; Reagents; Test specimens; Review of quality control data; Quality control logs, labeling of QC materials and reagents; Inventory control; Parallel testing; Water quality testing.

Examples of situations requiring investigation and remedial action as follows:

- Recurrent specimen collection/transportation problems.
- Microbial contamination in short- or long-term cultures.
- Major decline in slide quality due to problems with culturing, harvesting, or slide-making.
- Specimen misidentification or cross-contamination.
- Excessive turnaround time (TAT).
- Failure to meet current analytic standards.
- Client complaints or requests for amended reports.
- Trends of decline in test success rates. A trend can be defined as the percent of success below, for example: 98% for amniotic fluid and CVS (chorionic villus sampling) specimens; 60% for tissues; 95% for blood; 80% for hematological studies (blood and bone marrows).

The minimum success rates for adequate quality samples are as follows: amniotic fluid and long-term CVS (98%); direct CVS (90%); postnatal peripheral blood (98%); fetal blood (98%); conceptus/fetal parts/skin (60%); hematological malignancies (90%).

For adequate TAT, over 90% of test cases must be fianlly reported within the TAT.

- Preliminary report (verbal or written), STAT analyses: 3 days
- Fianl report STAT analyses: 7 days
- Fianl report, amniotic fluid and CVS: 14 days
- Final report, non-neoplastic blood analyses: 28 days
- Final report, neoplastic blood and bone marrow analyses: 21 days
- Final report, non-neoplastic fibroblast analyses: 6 weeks

2. Individualized QC plan (IQCP)

The Clinical Laboratory Improvement Amendment's (CLIA) new QC option called the IQCP applies to all non-waived testing performed. IQCP will allow laboratories to develop customized QC that is specific to the specific needs of the laboratory. Information and guidance to laboratories on IQCP can be found on the CLIA website: www.cms.hhs.gov/clia.

3. Standards of test records and reporting

The final test report must include the following items: the laboratory name; the patient name/sex; the patient's unique hospital number; the patient's age(birth date and year); the name of physician who request the test; the specimen type; the location where the specimen was obtained(if, necessary); sampling date/sample receipt date/test performed date; name of the person who performs the test/name of the person who reports the test results; report date; the signature of a qualified cytogeneticist; the test purpose; the number of metaphase cells counted, analyzed, and karyograms prepared; band resolution; banding method and resolution.

4. General culturing issues

All reagents, media, stains, and other materials shall be considered acceptable as long as the following criteria are met:

- Bacterial contamination is not observed in any culture of a properly collected specimen. Sporadic contamination can usually be traced to a failure of asceptic technique during initial specimen collection, over which we have no control.
- G-banding quality is such that interpretable karyotypes can be made consistently, and an adequate number of counts can be obtained.

5. Proficiency testing

Example of the ways to check accuracy of testing not part of an external PT as follows:

- Split a patient's specimen with another laboratory that offers the same test(s). Your director should review your results and the other laboratory's results for acceptability.
- Develop and perform internal PT on your laboratory assays in a blinded fashion. That is, take samples previously tested in your lab that has confirmed that the results are correct, and use these samples for future PTs. Lab personnel should not be informed of these samples being PTs and should not know the results of the original testing. See further for more details.
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· You must verify the accuracy of tests for which PT is required if any of the following occurs: 1) When your results are submitted to the program after the deadline and are considered a late submission, your laboratory grade will be zero; 2) If you did not test your PT samples at all, your laboratory grade will be zero.

6. Calibration verification

Calibration is not a standard process in cytogenetic labs except interphase FISH testing.

1) ACMG guideline for FISH calibration verification

(1) Metaphase analysis

E9.3 Biannual (twice per year) calibration or continuous quality monitoring verification is required based on CLIA requirements (42 CFR §493.1217) in the use of all FISH probes. This can be accomplished through a method of continuous monitoring of test results.

(2) Interphase analysis

E10.4 Biannual (twice per year) calibration or continuous quality monitoring is required to ensure that assay analytical sensitivity and specificity remain at the levels established during initial validation. Results that fall outside of the reportable range should be repeated. Continual test results that are outside of reportable ranges should be reassessed.

2) Calculating the normal/abnormal cutoff reference ranges for FISH probes

Normal results of a minimum of 20 cases for each FISH probe will be evaluated by the cytogenetics director to verify the accuracy of the established normal cutoff values. Normal cutoff is determined by using a formula that calculates the upper limit of the 95th percentile of the binomial distribution using beta-inverse function in an Excel program.

7. Laboratory developed tests (LDTs) of FISH assyas

The validation of LDTs include analytical performance (accuracy or correlation, precision, linearity or reportable range, limit of detection (LOD) and limit of quantification (LOQ), stability, interference,etc) and clinical performance (sensitivity, specificity, positive predictive value, negative predictive value).

Clinical and Laboratory Standards Institute (CLSI) document MM07-A2 recommended steps for FISH test implementation include optimization, probe localization, sensitivity, specificity, normal cutoffs, and establishment of normal, abnormal, and inconclusive criteria before analysis.

Accuracy of FISH tests could be validated by sensitivity and specificity of probes. Precision of FISH tests could be evaluated by reproducibility. But the acceptable range of precision of FISH test is difficult to obtain because of numerous variant signal patterns and the mosaicism. Ongoing monitoring of inter-observer reproducibility can be helpful. LOD and LOQ and reportable range of FISH can be evaluated with normal cutoff.

References

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