In today’s global society, mutual recognition of quality medical laboratory results is essential. ISO 15189 is an internationally recognized standard developed specifically for medical laboratories. It provides a mechanism for regulating bodies and accreditation agencies to confirm a laboratory’s competence in meeting technical and management requirements consistent with delivery of quality test results. Laboratories not specifically seeking accreditation also use ISO 15189 to implement good laboratory practices and assess their own competence.

ISO 15189 uses a quality management system framework to present interrelated management and technical requirements for all specialty areas of medical laboratory testing. Objectives of this standard include building, implementing and maintaining a quality system to assist medical laboratories in effectively organizing their operations to meet the quality requirements and expectations of clients, ensuring quality test results, and consistently improving the delivery and value of their services. The management requirements (clause 4) focus on organization and management responsibilities. The technical requirements (clause 5) address personnel, accommodation and environmental conditions, equipment, and the three phases – pre-analytical, analytical and post-analytical – of the testing process.

The following information identifies how ACL TOP® Hemostasis Testing Systems assist laboratories in meeting selected ISO 15189 technical requirements. ACL TOP systems are fully automated, bench-top, random-access, multi-parameter hemostasis analyzers from Instrumentation Laboratory (IL). They are designed specifically for in vitro diagnostic testing to assess hemostasis. ACL TOP systems include many capabilities to support the increasing demands of medium- and high-volume medical testing laboratories while increasing the quality and safety of testing and reducing many of the time-consuming tasks associated with the testing process.

In summary, the versatile platform of the ACL TOP Family of analyzers can be tailored for the needs of each medical laboratory. The many features – user-defined, automated quality control execution and assessment, onboard User Manual, configurable and controlled user access, maintenance and system usage logs, comprehensive report-generation – all help medical laboratories comply with numerous technical requirements of ISO 15189.

Meeting the Requirements of ISO 15189:2012 with ACL TOP Systems

In complying with the ISO 15189 technical requirements, features included in diagnostic systems can play a key role. The ACL TOP Family of analyzers are specifically designed to assist medical laboratories in meeting selected technical requirements highlighted below.

5.3.1. EQUIPMENT

5.3.1.2 Equipment acceptance testing

The laboratory shall verify upon installation and before use that the equipment is capable of achieving the necessary performance and that it complies with requirements relevant to any examination.

A note has been added to this section that states this requirement also includes equipment used in the laboratory on loan, or used in associated or mobile facilities by others authorized by the laboratory. See sections below for further discussion.

The following information includes features such as assay-specific information, including performance specifications, operation and maintenance for the company-validated and protected assay procedures that are pre-loaded on ACL TOP systems. These systems are password-protected. Laboratories can assign access to the analyzers based on laboratory-defined criteria, such as permitting only trained and authorized personnel to operate the instrument. See sections below for further discussion. The electronic User Manual is onboard all ACL TOP systems for easy access.
5.3.1.4 Equipment calibration and metrological traceability

The laboratory shall have a documented procedure for the calibration of equipment that directly or indirectly affects examination results. This procedure includes:

a) taking into account conditions of use and the manufacturer’s instructions;

- The US FDA-cleared Intended Use statement for ACL TOP systems is included in the User Manual.
- Manufacturer’s Instructions for the pre-loaded assay procedures are in the product insert sheets.

b) recording the metrological traceability of the calibration standard and the traceable calibration of the item of equipment;

- The calibration standard(s) are traceable to WHO Biological Reference Material when available, or to an alternative in-house standard. The current WHO Reference Material lot numbers (when available) are listed on each HemosIL® Calibration Plasma insert sheet.
- Up to 10 previous calibrations for each assay are stored onboard with traceability to materials used (e.g., lot numbers) and the operator who conducted the calibration.

c) verifying the required measurement accuracy and the functioning of the measuring system at defined intervals;

- ACL TOP systems can be configured to execute QC automatically at defined levels and frequency.

b) recording the calibration status and date of recalibration;

- For each assay, up to 10 calibrations along with date, time, and operator are maintained onboard.

e) ensuring that, where calibration gives rise to a set of correction factors, the previous calibration factors are correctly updated;

- When a calibration is validated by the user, the previous calibration and associated factors are no longer used.

f) safeguards to prevent adjustments or tampering that might invalidate examination results:

- ACL TOP pre-loaded test parameters are locked and cannot be altered by the operator.
- ACL TOP systems prevent alteration of test results.
- Security and all critical actions are logged automatically.

5.3.1.5 Equipment maintenance and repair

The laboratory shall have a documented program of preventive maintenance which, at a minimum, follows the manufacturer’s instructions. At a minimum, manufacturer’s schedules or instructions, or both, shall be used.

- All required maintenance activities for ACL TOP systems are listed in the User Manual and readily accessible on the software.
- ACL TOP systems flag assay results until the required maintenance is completed.

5.5 EXAMINATION PROCESSES

5.5.1 Selection, verification and validation of examination procedures

The laboratory shall select examination procedures which have been validated for their intended use (see 5.5.1.2). The identity of persons performing activities in examination processes shall be recorded. The specified requirements (performance specifications) for each examination procedure shall relate to the intended use of that examination.

(Note: Preferred procedures are those specified in the instructions for use of in vitro medical devices or those that have been published in established/authoritative textbooks, peer-reviewed

- Block further test analysis when QC fails or is overdue.
- Retrievable statistical information.
- QC results are stored onboard and are traceable to operator and material-lot information. The laboratory can customize and utilize the auto-validation features. All results that meet the selected criteria are transmitted to the information system for clinical validation, while those that do not are retained for review and validation.

5.7 POST-EXAMINATION PROCESSES

5.7.1 Review of results

The laboratory shall have procedures to ensure that authorized personnel review the results of examinations before release and evaluate them against internal quality control and, as appropriate, available clinical information and previous examination results. When the procedure for reviewing results involves automatic selection and reporting, review criteria shall be established, approved and documented (see section 5.9.1). Laboratories are required to have procedures that ensure the review of test results against internal quality control information, conformity with available patient clinical information, and previous examination results (when available) by authorized personnel before allowing the release of the results.

ACL TOP systems facilitate and enhance the efficiency of the technical review of results. Results are easily accessible and accompanied by laboratory-defined ranges (e.g., reference, therapeutic) and those defined by H (e.g., linear range). In addition, there are sophisticated data checks available for identifying unusual reactions. The laboratory can customize and utilize the auto-validation features. All results that meet selected criteria are transmitted to the information system for clinical validation, while those that do not are retained on the system for review and validation.
To support independent verifications, IL provides specific analytical assay information in the insert sheets for reagents, calibrators, and controls. Laboratories decide what data to collect to independently confirm that the manufacturer’s performance claims are met. Typically, test sites obtain objective evidence from studies designed to assess the method’s accuracy, precision, and linearity or reportable range/analytical measurement range.

5.5.1.3 Validation of examination procedures

Validated examination procedures used without modification shall be subject to independent verification by the laboratory before being introduced into routine use. The laboratory shall obtain information from the manufacturer/method developer for confirming the performance characteristics of the procedure.

The independent verification by the laboratory shall conform, through obtaining objective evidence (in the form of performance characteristics) that the performance claims for the examination procedure have been met. The performance claims for the examination procedure confirmed during the verification process shall be those relevant to the intended use of the examination results.

5.5.1.2 Verification of examination procedures

For all IL assays pre-loaded on ACL TOP systems, critical parameters cannot be modified (e.g., sample/reagent and test method volumes, incubation/reaction times, reading wavelengths, data reduction algorithms, and data checks).

To support independent verifications, IL provides specific information, including performance specifications, in insert sheets for reagents, calibrators, and controls.

Labs shall define the biological reference intervals or clinical decision values, document the basis for the reference intervals or decision values and communicate this information to users.

5.5.2 Biological reference intervals or clinical decision values

The laboratory shall define the biological reference intervals or clinical decision values, document the basis for the reference intervals or decision values and communicate this information to users.

• Reference intervals appropriate for the population served by the clinical laboratory should be selected. Laboratories can determine these experimentally or select them from a variety of sources. Examples of reference intervals are included in the IL product inserts.

5.5.3 Documentation of examination procedures

Examination procedures shall be documented. They shall be written in a language commonly understood by the staff in the laboratory and be available in appropriate locations. Any condensed document format (e.g., card files or similarly used systems) shall correspond to the documented procedure.

The laboratory is required to assemble a procedure manual that describes the entire testing process (5.5.3 sections a–t, when applicable). ISO 15189 requirements now include patient preparation, instructions for determining quantitative results when the result is outside the measurement interval, and references.

5.6 Quality control

5.6.2 Quality control materials

5.6.2.2 Quality control materials

The laboratory shall use quality control materials that react to the examining system in a manner as close as possible to patient samples. Quality control materials shall be periodically examined with a frequency that is based on the stability of the procedure and the risk of harm to the patient from an erroneous result.

The laboratory is required to develop QC policies and procedures including the appropriate control levels, control rules for result evaluation and frequency of control analysis.

• IL has multiple levels of QC materials, suitable for all ACL TOP systems. ACL TOP software allows for user-defined QC analysis and automatic evaluation of results.

• ACL TOP systems allow users to:
  ○ Configure automatic QC analysis by time of day, reagent vial change, and/or after a pre-defined number of tests.
  ○ Block further test analysis when QC fails or is overdue.

5.6.2.3 Quality control data

The laboratory shall have a procedure to prevent the release of patient results in the event of quality control failure. When the quality control rules are violated and indicate that examination results are likely to contain clinically significant errors, the results shall be rejected and relevant patient samples re-examined. Laboratory shall also evaluate the results from patient samples that were examined after the last successful quality control event. Quality control data shall be reviewed at regular intervals to detect trends in examination performance that may indicate problems in the examination system. When such trends are noted, preventive actions shall be taken and recorded.

(Note: Statistical and non-statistical techniques for process control should be used wherever possible to continuously monitor examination system performance.)

• Onboard QC on ACL TOP systems allows users to:
  ○ Configure automatic QC analysis by time of day, reagent vial change, and/or after a pre-defined number of tests.
  ○ Block or flag patient results when QC is overdue or fails.
5.5.1.2 Verification of examination procedures

Validated examination procedures used without modification shall be subject to independent verification by the laboratory before being introduced into routine use. The laboratory shall obtain information from the manufacturer/method developer for confirming the performance characteristics of the procedure.

The independent verification by the laboratory shall confirm, through obtaining objective evidence (in the form of performance characteristics) that the performance claims for the examination procedure have been met. The performance claims for the examination procedure have been met. The laboratory defines which system functions are accessible to individual operators. Only authorized operators (e.g., those who have been trained and have proven competence) may log-on and operate the system according to their individual access rights.

All critical operations, including user log-on and log-off, are automatically documented by ACL TOP systems for full traceability. These systems track events and actions to operators logged in when the event or action occurs.

5.5.1.3 Validation of examination procedures

(Note: This section is only relevant for non-standard, laboratory/user-defined, and modified methods.)

Test parameters defined by IL cannot be modified.

5.5.2 Biological reference intervals or clinical decision values

The laboratory shall define the biological reference intervals or clinical decision values, document the basis for the reference intervals or decision values and communicate this information to users.

- Reference intervals appropriate for the population served by the clinical laboratory should be selected. Laboratories can determine these experimentally or select them from a variety of sources. Examples of reference intervals are included in the IL product inserts.

5.5.3 Documentation of examination procedures

Examination procedures shall be documented. They shall be written in a language commonly understood by the staff in the laboratory and be available in appropriate locations. Any condensed document format (e.g., card files or similarly used systems) shall correspond to the documented procedure.

The laboratory is required to assemble a procedure manual that describes the entire testing process (5.5.3 sections a-t, when applicable). ISO 15189 requirements now include patient preparation, instructions for determining quantitative results when the result is outside the measurement range, and references.

- For all IL assays pre-loaded on ACL TOP systems, critical parameters cannot be modified (e.g. sample/reagent and test method volume, incubation/reaction times, reading wavelengths, data reduction algorithms, and data checks).

- To support independent verifications, IL provides specific information, including performance specifications, in insert sheets for reagents, calibrators, and controls. Laboratories decide what data to collect to independently confirm that the manufacturer’s performance claims are met. Typically, test sites obtain objective evidence from studies designed to assess the method’s accuracy, imprecision, and linearity or reportable range/analytical measurement range.

5.5.3.3 Validation of examination procedures

The laboratory shall design quality control procedures that verify the attainment of the intended quality of results.

(Note: In several countries, quality control, as referred to in this subclause, is also named “internal quality control.”)

The laboratory is required to develop QC policies and procedures, including appropriate control levels, control rules and frequency of control analysis, to verify the attainment of the intended quality of the results.

- ACL TOP systems have sophisticated onboard QC options, which provide the laboratory with tools for meeting this requirement.

- Onboard QC on ACL TOP systems allows users to:
  - Select from integrated QC Westgard multi-rules.
  - Block patient results when QC is overdue or fails.
  - Configure automatic QC analysis by time, reagent vial change, and/or after a pre-defined number of tests.
  - Block further test analysis when QC fails or is overdue.

5.6 ENSURING QUALITY OF EXAMINATION RESULTS

5.6.2 Quality control

5.6.2.1 General

The laboratory shall have a procedure to prevent the release of patient results in the event of quality control failure. When the quality control rules are violated and indicate that examination results are likely to contain clinically significant errors, the results shall be rejected and relevant patient samples re-examined. Laboratory shall also evaluate the results from patient samples that were examined after the last successful quality control event. Quality control data shall be reviewed at regular intervals to detect trends in examination performance that may indicate problems in the examination system. When such trends are noted, preventive actions shall be taken and recorded.

(Note: Statistical and non-statistical techniques for process control should be used wherever possible to continuously monitor examination system performance.)

- Onboard QC on ACL TOP systems allows users to:
  - Configure automatic QC analysis by time of day, reagent vial change, and/or after a pre-defined number of tests.
  - Block or flag patient results when QC is overdue or fails.
5.3.1.4 Equipment calibration and metrological traceability

The laboratory shall have a documented procedure for the calibration of equipment that directly or indirectly affects examination results. This procedure includes:

a) taking into account conditions of use and the manufacturer’s instructions;

• The US FDA-cleared Intended Use statement for ACL TOP systems is included in the User Manual.

• Manufacturer’s Instructions for the pre-loaded assay procedures are in the product insert sheets.

b) recording the metrological traceability of the calibration standard and the traceable calibration of the item of equipment;

• The calibration standard(s) are traceable to WHO Biological Reference Material when available, or to an alternative in-house standard. The current WHO Reference Material lot numbers (when available) are listed on each HemosIL® Calibration Plasma insert sheet.

• Up to 10 previous calibrations for each assay are stored onboard with traceability to materials used (e.g., lot numbers) and the operator who conducted the calibration.

c) verifying the required measurement accuracy and the functioning of the measuring system at defined intervals;

• ACL TOP systems can be configured to execute QC automatically at defined levels and frequency.

d) recording the calibration status and date of recalibration;

• For each assay, up to 10 calibrations along with date, time, and operator are maintained onboard.

e) ensuring that, where calibration gives rise to a set of correction factors, the previous calibration factors are correctly updated;

• When a calibration is validated by the user, the previous calibration and associated factors are no longer used.

f) safeguards to prevent adjustments or tampering that might invalidate examination results.

• ACL TOP pre-loaded test parameters are locked and cannot be altered by the operator.

• ACL TOP systems prevent alteration of test results.

• Security and all critical actions are logged automatically.

5.3.1.5 Equipment maintenance and repair

The laboratory shall have a documented program of preventive maintenance which, at a minimum, follows the manufacturer’s instructions. At a minimum, manufacturer’s schedules or instructions, or both, shall be used.

• All required maintenance activities for ACL TOP systems are listed in the User Manual and readily accessible on the software. Most of the maintenance activities are fully or semi-automated to minimize the need for user intervention and dedicated maintenance time. The system alerts the operator when an activity is due and documents the date and execution time of each maintenance activity. If an activity becomes overdue, ACL TOP systems flag assay results until the required maintenance is completed.

5.5 EXAMINATION PROCESSES

5.5.1 Selection, verification and validation of examination procedures

The laboratory shall select examination procedures which have been validated for their intended use (see 5.5.1.2). The identity of persons performing activities in examination processes shall be recorded. The specified requirements (performance specifications) for each examination procedure shall relate to the intended use of that examination.

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