COLLEGE of AMERICAN PATHOLOGISTS

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Hematology and Coagulation Checklist

CAP Accreditation Program

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Hematology and Coagulation Checklist

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ON-LINE CHECKLIST DOWNLOAD OPTIONS

Participants of the CAP accreditation programs may download the checklists by logging into cap.org and going to e-LAB Solutions Suite - Accreditation Checklists. They are available in different checklist types and formatting options, including:

- Master — contains ALL of the requirements and instructions available in PDF, Word/XML or Excel formats
- Custom — customized based on the laboratory's activity (test) menu; available in PDF, Word/XML or Excel formats
- Changes Only — contains only those requirements with significant changes since the previous checklist edition in a track changes format to show the differences; in PDF version only. Requirements that have been moved or merged appear in a table at the end of the file.

CHECKLIST ACCREDITATION RESOURCES

CAP accredited laboratories have access to additional checklist accreditation tools and resources found on the CAP website (cap.org) by logging into e-LAB Solutions Suite - Accreditation Resources. Content found in Accreditation Resources includes:

- A library of past Focus on Compliance webinars and laboratory inspection preparation videos
- Answers to the most common checklist questions
- Customizable templates and forms (eg, competency assessment, personnel, validation/verification, quality management)
- Proficiency testing (PT) frequently asked questions, forms, and troubleshooting guides
- IQCP eligibility, frequently asked questions, forms, templates, and examples
- Laboratory director education and resources
- Quality management resources
- Inspector training and inspection tip sheets
- Self and post inspection toolbox

SUMMARY OF CHECKLIST EDITION CHANGES
Hematology and Coagulation Checklist
12/26/2024 Edition

The information below includes a listing of checklist requirements with significant changes in the current edition and previous edition of this checklist. The list is separated into three categories:

1. New
2. Revised:
   - Modifications that may require a change in policy, procedure, or process for continued compliance; or
   - A change to the Phase
3. Deleted/Moved/Merged**:**
   - Deleted
   - Moved — Relocation of a requirement into a different checklist (requirements that have been resequenced within the same checklist are not listed)
   - Merged — The combining of similar requirements

NOTE: The requirements listed below are from the Master version of the checklist. The customized checklist version created for inspections and self-evaluations may not list all of these requirements.

Previously Cited Checklist Requirements

- The **inspector's version** of the checklist contains a listing of previously cited checklist requirements. Specific information on those citations, including the inspection date and inspector comments, is included following each related requirement within the checklist.
- Laboratories can access data on previously cited deficiencies by logging into e-LAB Solutions Suite on cap.org and going to Accreditation Reports - Inspection Summation Report.

NEW Checklist Requirements

Requirement	Effective Date
HEM.36960	12/26/2024

REVISED Checklist Requirements

Requirement	Effective Date
HEM.36820	12/26/2024
HEM.36880	12/26/2024
HEM.36920	08/24/2023
HEM.37165	08/24/2023
HEM.37373	08/24/2023
HEM.37375	08/24/2023

DELETED/MOVED/MERGED Checklist Requirements
None

INTRODUCTION

This checklist is used in conjunction with the All Common and Laboratory General Checklists to inspect a hematology laboratory section or department.

Certain requirements are different for waived versus nonwaived tests. Refer to the checklist headings and explanatory text to determine applicability based on test complexity. The current list of tests waived under CLIA may be found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm.


Policy/Procedure icon - The placement of this icon next to a checklist requirement indicates that a written policy or procedure is required to demonstrate compliance with the requirement. The icon is not intended to imply that a separate policy or procedure is required to address individual requirements. A single policy or procedure may cover multiple checklist requirements.

Laboratories not subject to US regulations: *Checklist requirements apply to all laboratories unless a specific disclaimer of exclusion is stated in the checklist. When the phrase "FDA-cleared/approved test (or assay)" is used within the checklist, it also applies to tests approved by an internationally recognized regulatory authority (eg, CE-marking).*

QUALITY CONTROL

WAIVED TESTS - GENERAL

HEM.18038 QC - Waived Tests **Phase II**

The laboratory follows manufacturer's instructions for quality control, reviews results, and records acceptability prior to reporting patient results.

NOTE: Quality control must be performed according to manufacturer's instructions. To detect problems and evaluate trends, testing personnel or supervisory staff must review quality control data on days when controls are run prior to reporting patient results. The laboratory director or designee must review QC data at least monthly or more frequently if specified in the laboratory QC policy.

*With respect to internal controls, acceptable control results must be recorded, at a minimum, once per day of patient testing for each device.**

**Acceptable internal control results need not be recorded, if (and only if) an unacceptable instrument control automatically locks the instrument and prevents release of patient results.*

Evidence of Compliance:

- ✓ Records showing confirmation of acceptable QC results

HEM.18691 QC Corrective Action - Waived Tests **Phase II**

The laboratory performs and records corrective action when control results exceed defined acceptability limits.

HEM.18705 Calibration, Calibration/Verification - Waived Tests **Phase II**

For waived tests, the laboratory follows manufacturer's instructions for calibration, calibration verification, and related functions.

Evidence of Compliance:
- ✓ Records for calibration/calibration verification/related functions as required by the manufacturer **AND**
- ✓ Records of recalibration or other appropriate corrective action when calibration verification is unacceptable

NOTE: The remaining requirements in this checklist on controls, calibration, and reportable range do not apply to waived tests.

NONWAIVED TESTS - GENERAL

The following group of requirements is applicable to nonwaived manual, automated, and semi-automated testing, unless a separate checklist requirement exists in another checklist section that defines a specific QC frequency (eg, CBC instrument, coagulation testing, manual cell counts).

HEM.19360 Daily QC - Nonwaived Tests **Phase II**

The laboratory performs controls for quantitative and qualitative tests each day of testing, or more frequently if specified in manufacturer's instructions, laboratory procedure, or the CAP Checklist, and when changes occur that may impact patient results.

NOTE: The laboratory must define the number and type of quality control used and the frequency of testing in its quality control procedures. Control testing is not required on days when patient testing is not performed.

Controls must be run prior to resuming patient testing when changes occur that may impact patient results, including after a change of analytically critical reagents, major preventive maintenance, change of a critical instrument component, or with software changes, as appropriate.

Daily quality control must be run as follows:
- *Quantitative tests - two controls at different concentrations at least daily, except for coagulation tests (two controls every eight hours), or unless otherwise required elsewhere in this checklist*
- *Qualitative tests - a negative control and a positive control (when applicable) at least daily*

Controls should verify assay performance at relevant decision points. The selection of these points may be based on clinical or analytical criteria.

If an internal quality control process (eg, electronic/procedural/built-in) is used instead of an external control material to meet daily quality control requirements, the laboratory must have an individualized quality control plan (IQCP) approved by the laboratory director defining the control process, including the frequency and use of external and internal controls. At a minimum, external control materials must be analyzed with new lots and shipments of reagents or more frequently if indicated in the manufacturer's instructions. Please refer to the IQCP section of the All Common Checklist for the eligibility of tests for IQCP and requirements for implementation and ongoing monitoring of an IQCP.

Evidence of Compliance:
- ✓ Records of QC results including external and internal control procedures **AND**
- ✓ Manufacturer product insert or manual

HEM.19380 Control Range Establishment or Verification **Phase II**

The laboratory establishes or verifies an acceptable control range for each lot of control material.

NOTE: For unassayed control materials, the laboratory must establish an acceptable control range by repetitive analysis in runs that include previously tested control material. For assayed control materials, the laboratory must verify control ranges supplied by the manufacturer.

Control values supplied by the manufacturer may be used without verification for qualitative (eg, positive or negative) testing.

Evidence of Compliance:

- ✓ Records for control range establishment or verification of each lot

HEM.20050 Numeric QC Data **Phase II**

For numeric QC data, quality control statistics (eg, SD and CV) are calculated monthly to define and monitor analytic imprecision.

NOTE: For CBC data where stabilized whole blood is not used for quality control, such statistics may be generated from previous patient samples using the standard deviation of duplicate pairs.

Evidence of Compliance:

- ✓ QC records showing monthly monitoring of imprecision

HEM.20070 Precision Statistics **Phase I**

The laboratory has an action protocol when data from precision statistics change significantly from previous data.

NOTE: As an example, if the laboratory's normal-level commercial control usually yields a monthly CV of 2% for WBC, but the most recent month shows a 4% CV, then something has caused increased imprecision, and investigation with records is required. Similarly, if the monthly SD for MCV by moving averages is typically around 1.8 fL, but now is at 3.1 fL, the laboratory must find a cause for this shift and take action. If commercially sponsored interlaboratory QC data for the same control lot and instrument model show SD/CV values outside those of the peer group, an explanation is required.

Evidence of Compliance:

- ✓ Records of investigation and corrective actions taken

HEM.20090 Alternative Control Procedures **Phase II**

If the laboratory performs test procedures for which control materials are not commercially available, the laboratory performs and records alternative control procedures to detect immediate errors and monitor test system performance over time.

NOTE: "Performance" includes elements of accuracy, precision, and clinical discriminating power. The following are examples of alternative procedures: split sample testing with another method or with another laboratory, the testing of previously tested patient specimens in duplicate, testing of patient specimens in duplicate, or other defined processes approved by the laboratory director.

Evidence of Compliance:

- ✓ Records of alternative control procedures

HEM.20120 QC Handling **Phase II**

The laboratory tests control specimens in the same manner and by the same personnel as patient samples.

NOTE: Personnel who routinely perform patient testing must analyze QC specimens; however, this does not imply that each operator must perform QC daily. Personnel must participate in QC on a regular basis. To the extent possible, all steps of the testing process must be controlled.

Evidence of Compliance:
- ✓ Records reflecting that QC is performed by the same personnel performing patient testing

HEM.20140 QC Confirmation of Acceptability **Phase II**

Personnel review control results for acceptability before reporting patient/client results.

Evidence of Compliance:
- ✓ Records of control result approval

HEM.20143 QC Corrective Action **Phase II**

The laboratory performs and records corrective action when control results exceed defined acceptability limits.

NOTE: The actions taken must be consistent with the laboratory's quality control program (GEN.30000). Patient test results obtained in an analytically unacceptable test run or since the last acceptable test run must be re-evaluated to determine if there is a significant clinical difference in patient/client results. Re-evaluation may or may not include re-testing patient samples, depending on the circumstances.

Even if patient samples are no longer available, test results can be re-evaluated to search for evidence of an out-of-control condition that might have affected patient results. For example, evaluation could include comparison of patient means for the run in question to historical patient means, and/or review of selected patient results against previous results to see if there are consistent biases (all results higher or lower currently than previously) for the test(s) in question.

The corrective action for tests that have an IQCP approved by the laboratory director must include an assessment of whether further evaluation of the risk assessment and quality control plan is needed based on the problems identified (eg, trending for repeat failures, etc.).

Evidence of Compliance:
- ✓ Records of corrective action for unacceptable control results

HEM.20146 Monthly QC Review **Phase II**

The laboratory director or designee reviews and assesses quality control data at least monthly.

NOTE: The reviewer must record follow-up for outliers, trends, or omissions that were not previously addressed.

The QC data for tests performed less frequently than once per month may be reviewed when the tests are performed.

The review of quality control data for tests that have an IQCP approved by the laboratory director must include an assessment of whether further evaluation of the risk assessment and quality control plan is needed based on problems identified (eg, trending for repeat failures, etc.).

Evidence of Compliance:
- ✓ Records of QC review **AND**
- ✓ Records of corrective action taken when acceptability criteria are not met

HEMATOLOGY

SPECIMEN COLLECTION AND HANDLING

HEM.22000 Collection in Anticoagulant **Phase II**

All blood specimens collected in anticoagulant for hematology testing are mixed thoroughly immediately before analysis.

NOTE: Some rocking platforms may be adequate to maintain even cellular distribution of previously well-mixed specimens, but are incapable of fully mixing a settled specimen. For instruments with automated samplers, the laboratory must ensure that the automated mixing time is sufficient to homogeneously disperse the cells in a settled specimen.

Evidence of Compliance:

- ✓ Records of evaluation of each specimen mixing method (eg, rotary mixer, rocker, automated sampler, or manual inversions) for reproducibility of results, as applicable

HEM.22050 CBC Anticoagulant **Phase II**

Samples for complete blood counts and blood film morphology are collected in potassium EDTA.

NOTE: Blood specimens for routine hematology tests (eg, CBC, leukocyte differential) must be collected in potassium EDTA to minimize changes in cell characteristics. Laboratories must follow manufacturer's recommendations for use of alternative anticoagulants.

HEM.22100 Capillary Tube Collection Criteria **Phase II**

Samples collected in capillary tubes for microhematocrits or capillary/dilution systems are obtained in duplicate whenever possible.

NOTE: Microspecimen containers such as those used for other capillary blood CBC parameter determinations need not be collected in duplicate. Because of the risk of injury, the use of glass capillary tubes is discouraged; if glass capillary tubes are used, measures have been implemented to reduce risk or injury.

HEM.22150 Specimen Quality Assessment - CBC **Phase II**

CBC specimens are checked for clots (visual, applicator sticks, or automated analyzer histogram inspection/flags) before reporting results.

NOTE: This may be done visually or with applicator sticks before testing. Additionally, microclots will often present themselves histographically on automated and semi-automated particle counters or by flagging, and the testing personnel must become familiar with such patterns. Finally, platelet clumps or fibrin may be microscopically detected if a blood film is prepared on the same sample.

HEM.22200 Hemolyzed or Lipemic Specimens - CBC **Phase II**

CBC specimens are checked for significant in vitro hemolysis and possible interfering lipemia before reporting results.

NOTE: Specimens for complete blood counts must be checked for in vitro hemolysis that may falsely lower the erythrocyte count and the hematocrit, as well as falsely increase the platelet concentration from erythrocyte stroma. Visibly red plasma in a tube of EDTA-anticoagulated settled or centrifuged blood should trigger an investigation of in vivo hemolysis (in which case the CBC data are valid) versus in vitro hemolysis (in which case some or all of the CBC data are not valid and should not be reported). Lipemia may adversely affect the hemoglobin concentration and the leukocyte count. This does not imply that every CBC specimen must be subjected to centrifugation with visual inspection of the plasma supernatant, particularly if this would significantly impair the laboratory's turnaround time. An acceptable alternative for high volume laboratories with automated instrumentation is to examine the numeric data for anomalous results (especially indices), as well as particle histogram inspection.

HEM.22625 Storage and Stability - Hematology **Phase I**

The laboratory defines sample storage conditions and stability for all hematology parameters.

NOTE: The laboratory must define sample storage conditions and stability for all hematology parameters, as time- and temperature-dependent alterations can occur, creating spurious results.

COMPLETE BLOOD COUNT (CBC) INSTRUMENTS

CALIBRATION

Commercially available calibrator materials represent a convenient way to ensure that CBC instruments yield accurate results. Because of differences in technology, such calibrators are typically instrument-specific, and are cleared by the Food and Drug Administration for such use. These calibrators have more rigorous assignment of target values than ordinary commercial QC materials. Commercial control materials are not suitable for routine instrument calibration.

HEM.25400 Precalibrated Instrument Verification **Phase II**

If precalibrated instruments are used, the manufacturer's calibrations are verified with appropriate control materials for the system.

NOTE: This requirement does not apply to CBC instruments that can be calibrated by the laboratory.

Evidence of Compliance:
- ✓ Records of calibration verification following manufacturer's instructions

HEM.25700 Calibration **Phase II**

The laboratory follows defined criteria for periodic analyzer calibration using stabilized materials with target values certified by the manufacturer using primary reference procedures.

HEM.25760 Calibration Verification Criteria **Phase II**

Criteria for the frequency and acceptability of calibration verification are defined and followed.

NOTE: Criteria for calibration verification include:
1. *At complete changes of reagents (ie, change in type of reagent from same vendor, or change to a different vendor)*
2. *When indicated by quality control data*
3. *After major maintenance or service*
4. *When recommended by the manufacturer*
5. *At least every six months*

For automated CBC cell counting instruments, requirements for calibration verification may be considered met if the laboratory follows the manufacturer's instructions for instrument operation and tests two levels of control materials each day of testing. The control results must meet the laboratory's criteria for acceptability. Linearity studies are not required.

Evidence of Compliance:
- ✓ Records of calibration verification at defined frequency

HEM.25780 Recalibration **Phase II**

The laboratory performs recalibration of parameters using stabilized whole blood or other commercial preparations with parameters certified by the manufacturer.

CBC INSTRUMENT QUALITY CONTROL

Longitudinal process quality control (QC) procedures for individual instruments may include:
1. *Use of preserved or stabilized whole blood controls*
2. *"Moving average" monitoring*
3. *Retained patient specimens, or*
4. *Some combination of the above*

At least two different controls must be assayed and evaluated every 24 hours. For each QC procedure employed, the laboratory must have appropriate QC ranges. For example, expected recovery ranges for commercial control materials are NOT the same as between-run SD ranges, and are probably too wide for daily QC of a single instrument. The laboratory should calculate its own imprecision statistics for each instrument.

STABILIZED CONTROLS

HEM.25850 Stabilized Controls **Phase II**

The laboratory analyzes two different stabilized control specimens during each 24-hours of analyzer use.

NOTE: Stabilized control materials must be at two different analytic levels (ie, "normal" and "high"). Three levels of control is a conceptual carryover from clinical chemistry, and does not apply to hematology particle counting. Dilute, "low-level" (eg, leukopenic and thrombocytopenic) "oncology" controls are less informative indicators of calibration status and are neither required nor recommended. For example, a 10% calibration bias will be numerically most apparent in a high-level control, less apparent in a normal-level control, and perhaps inapparent in a low-level control; it would be quite extraordinary for a low-level control to indicate a calibration problem that is not revealed by the other controls. There should be some relationship between the frequency

of control runs and the numbers of patient specimens processed. If the frequency of commercial control use is less than two control specimens per 24 hours, one or more of the additional approaches to QC must be employed to produce a total of at least two different data points per 24 hours.

Evidence of Compliance:
- ✓ Records of QC results

MOVING AVERAGES

The technique of weighted moving averages (derived from multiple batch analysis of patient samples) is acceptably sensitive to drifts or shifts in analyzer calibration if a supplemental QC routine (stabilized control material or retained patient specimens) is employed. The latter is needed to detect random error and to avoid bias due to masking of drift by characteristics of the subpopulations within each individual batch.

Laboratories analyzing fewer than 100 CBC specimens daily (long term average) should not use moving averages as the primary method for process control, as this would not generate sufficient data within a day to be of value.

Depending on the particular instrument, there may be "on-board" moving average analyses for RBC indices only. In such cases, additional QC techniques are required for WBC, PLT and WBC differential parameters. However, some laboratories have found the mathematical logic of moving averages, modified average of normals, etc., applicable to other CBC parameters, and some instruments have these capabilities built into their software. Or, such calculations may be performed with an associated computer.

HEM.25920 QC - Moving Averages **Phase II**

Control limits for moving averages are appropriately sensitive.

NOTE: Control limits for moving averages must be appropriately sensitive such that significant calibration alterations are always detected. The written procedures must define the method used to establish the moving average, the frequency of calculation (batch size), and criteria for selection of upper and lower limits.

Recalibration is not required for minor calibration variations of no clinical consequence. In other words, there should be a high probability for error detection and a low probability for false rejection.

HEM.25990 QC Procedure **Phase II**

If a "moving averages" system is combined with another control system (commercial controls or retained patient specimens), the process is well defined and appropriately sensitive to drift in analyzer calibration.

Evidence of Compliance:
- ✓ Records of QC results using moving averages

RETAINED PATIENT SPECIMENS

Use of retained patient specimens alone is inadequate for routine QC of the primary CBC instrument, and must be considered as a supplemental procedure, in combination with another QC system. Retained patient specimens, while conveniently available, present some difficulties in mathematically defining "agreement"

between CBC results separated in time, as these are not stabilized samples. This is in contrast to commercial control materials that have been treated to reduce time-dependent degradation.

HEM.26660 QC - Retained Patient Specimens **Phase I**

When the laboratory uses retained patient specimens, statistically defined limits are used to determine agreement of sequential assays of a given specimen.

NOTE: Allowance should be made for time-dependent alterations in data from such labile specimens.

Evidence of Compliance:
- ✓ QC records for retained patient specimens

HEM.27330 QC - CBC Defined Range **Phase I**

There is a defined range of CBC values for which control limits used for retained patient specimens are applicable.

NOTE: Because imprecision (standard deviation, coefficient of variation) is dependent upon the hematologic target value, limits must be restricted to appropriate ranges of CBC values.

ERROR DETECTION AND VERIFICATION

HEM.30070 Sampling Mode Comparison **Phase I**

The laboratory compares all results obtained for patient specimens analyzed in the multiple sampling modes of the CBC analyzer (eg, "primary" and "secondary" modes) at least annually to ensure that they are in agreement.

NOTE: Different modes may involve a different sample path before analysis. When samples are analyzed in more than one mode, it is important to ensure that all modes function properly. Re-analysis of a previously analyzed sample must be performed in the alternate mode(s), and results must agree with the initial mode within the tolerance limits established for agreement by the hematology laboratory's quality control program, and any recommendations by the instrument manufacturer. Mode-to-mode correlation is not necessary for those analyzers that use the same pathway for all modes.

Evidence of Compliance:
- ✓ Records of sampling mode comparison studies

HEM.30100 Detection/Correction Procedure - WBC **Phase II**

The laboratory has a process to detect and correct automated WBC counts for the presence of nucleated red cells or megakaryocytes.

NOTE: The effect of nucleated erythrocytes and blood megakaryocytes on the apparent WBC count varies with the system used for analysis. Each laboratory must evaluate its system(s) and develop appropriate detection and correction procedures. This is important to prevent reporting a falsely high WBC concentration. With some automated CBC instruments, nucleated erythrocytes or megakaryocytes may present themselves histographically or cytographically, and this can serve as an indicator for careful inspection of a stained blood film. The laboratory must establish if its particular instrument(s) includes some or all nucleated non-leukocytes in its apparent WBC "count".

Evidence of Compliance:
- ✓ Records showing actions taken to verify WBC concentration prior to reporting

HEM.30150 Spurious CBC Results **Phase II**

The laboratory has a process to detect spurious CBC instrument results that may be clinically significant (eg, pseudomacrocytosis from rouleaux or agglutinates; pseudoleukocytosis with erroneous hemoglobin, falsely low erythrocyte count and hematocrit; hyperlipemia) prior to reporting.

NOTE: Analytic sources of error with automated instruments depend on the type of instrument and reagents used by the laboratory.

Evidence of Compliance:
- ✓ Record of action taken when spurious CBC instrument results are detected

HEM.30200 Red Cell Indices **Phase I**

The laboratory routinely monitors red cell indices (MCV, MCH, MCHC) to detect random errors.

NOTE: Patient sample red cell indices (MCV, MCH, MCHC) must be monitored routinely to detect random errors, instrument malfunction, or spurious results. On many automated instruments, the MCHC is the most useful parameter to ensure accuracy of the red cell parameters in individual patient samples. Since MCHC varies over a narrow range, an abnormal MCHC will often flag potentially spurious red cell parameters. Truly elevated MCHCs may be seen with spherocytosis, while decreased MCHCs can accompany a low MCV in severe iron deficiency anemia. If such RBC abnormalities are not present on the blood film, one or more of the measured RBC parameters is likely erroneous. Incorrect data may be due to instrument malfunction or to problems with the blood sample itself. MCV and MCH are fairly constant for each patient, and monitoring these indices in a delta check error detection program may provide rapid patient-based detection of instrument malfunction or specimen misidentification.

Evidence of Compliance:
- ✓ Record of action taken when RBC indices are in question, including the reporting of results

HEM.30250 Reportable Range **Phase II**

Upper and lower limits of all reportable parameters on the CBC instrument are defined, and results that fall outside these limits are reported properly.

NOTE: The laboratory must initially establish or verify the reportable range for each parameter of its automated or semi-automated CBC instrument. In particular, the laboratory must have data on its instrument's accuracy with thrombocytopenic and leukopenic samples. Platelet concentrations below the established lower limits must be reanalyzed by another method (eg, manual hemocytometry, or semiquantitative blood film estimates, or fluorescence flow cytometry using specific platelet monoclonal antibodies). Particle (WBC, RBC, PLT) concentrations above the established upper limits must, as clinically needed, be reanalyzed by doing the minimum dilution necessary to bring the counts into the instrument's analytic range. When clinically appropriate, apparent analyte concentrations that are lower or higher than the reportable range may be reported as "less than" the lower limit or "greater than" the higher limit.

Evidence of Compliance:
- ✓ Record of action taken when limits are exceeded, including the reporting of results

HEM.30300 Platelet Abnormalities **Phase II**

The laboratory has a process (such as microscopic correlation with the blood film) to prevent reporting of spurious thrombocytopenia when platelet clumps, giant platelets, or platelet satellitism are present.

NOTE: When platelet satellitosis (satellitism), significant numbers of giant platelets and/or platelet clumps are suspected/detected by cyto/histographic abnormalities or instrument rejection of a platelet result, the platelet concentration must be independently verified. Correlation with a well-prepared blood film must be made. If platelets are clumped after collection in an EDTA-anticoagulated tube that was well-mixed at the time of collection, this may represent in vitro EDTA-induced changes; platelets must be quantified from blood collected directly into a counting diluent, by use of a different anticoagulant per manufacturer's recommendations, or by estimation from a non-anticoagulated blood film.

Evidence of Compliance:
- ✓ Record showing actions taken to verify platelet concentration prior to reporting

HEM.30350 Spuriously High WBC Concentration **Phase II**

If significant numbers of unlysed RBC, giant platelets and/or platelet clumps are suspected/detected, the WBC concentration is rechecked by another method or blood films are examined to prevent reporting spuriously high WBC concentrations.

NOTE: When unlysed RBC, PLT satellitosis, significant numbers of giant PLT and/or PLT clumps are suspected/detected by histographic abnormalities or instrument rejection of the PLT result, the WBC count must be verified manually, by automated counting after collection into a different anticoagulant, by automated counting in a lyse-resistant mode, or by semiquantitative blood film evaluation to prevent reporting spuriously high WBC concentrations.

Evidence of Compliance
- ✓ Record showing actions taken to verify WBC concentration prior to reporting

HEM.30400 Platelet Count Verification **Phase II**

If significant numbers of microcytic erythrocytes and/or small cell fragments are detected/ suspected, the platelet count is determined or verified using an alternate method.

NOTE: When a significant number of interfering particles are identified at the upper or lower PLT counting threshold (by inspection of the PLT histogram or instrument flag), the PLT concentration must be determined or verified by an alternate method. Such methods could include alternate instrumentation, hemocytometry, or blood film estimate, depending upon the PLT concentration and the degree of clinical accuracy required.

Evidence of Compliance:
- ✓ Records showing action taken to verify platelet concentration prior to reporting

AUTOMATED DIFFERENTIALS

HEM.34100 Acceptable Limits - WBC **Phase II**

Acceptable limits for quality control procedures for WBC subclasses using manually counted blood films or commercial controls are defined.

NOTE: For automated analyzers, at least two approaches are reasonable: 1) comparison of instrument differentials on fresh blood samples with a conventional manual differential count, and/or 2) use of commercially available stabilized leukocytes and/or particle surrogate control

material. The automated instrument and reference determinations should be treated as replicate manual differentials and evaluated using the ± 2 or 3 SD agreement limits of Rümke. For pattern recognition microscopy systems, QC can be done by periodic processing of prepared control slides and maintenance/analysis of Levey-Jennings charts.

For commercial controls, mixed leukocyte subclasses (eg, "mononuclear" or "large unclassified cells") or "remainder" fractions do not need to be assessed with QC procedures. The commercial material must contain surrogate particles to measure total neutrophils, total granulocytes, total lymphoid cells, monocytes, eosinophils, and basophils, if these subtypes are enumerated by the instrument and reported by the laboratory. If discrete populations of abnormal cells are identified and enumerated by the instrument (eg, nucleated RBC, blasts), then the QC material must contain surrogate particles to evaluate accuracy.

HEM.34200 WBC Differential Verification **Phase II**

The laboratory uses defined criteria for review and evaluation of leukocyte differential counter data, histograms, and/or blood films for clinically important results flagged by the automated differential counter.

NOTE: Clinically important results include pathologic quantities of normal cell types and abnormal cells. Flagging mechanisms include those within the particular instrument, inspection of histographic/cytographic displays, laboratory criteria based on local experience, and awareness of published evaluations.

Evidence of Compliance:
- ✓ Records of verification of flagged values

MANUAL DIFFERENTIALS

This section applies to all manually interpreted differentials, including those performed using automated image analysis systems requiring manual verification or interpretation of cell classification or other morphologic findings.

HEM.34300 Blood Film Quality **Phase I**

The quality of blood films is satisfactory (properly stained, free of precipitate, good cell distribution).

HEM.34320 Stain Reactivity **Phase II**

All stains are checked for intended reactivity each day of use.

Evidence of Compliance:
- ✓ Records of stain QC at defined frequency

HEM.34400 Morphologic Observation Evaluation - CBC **Phase II**

The laboratory evaluates consistency of morphologic observation among personnel performing blood cell microscopy at least annually.

NOTE: The laboratory must ensure the identification and morphology of blood cells is reported consistently amongst all personnel performing the microscopic analysis.

Suggested methods to accomplish this include:

1. *Circulation of a pre-graded set of blood films with defined leukocyte differential distributions, and RBC and platelet morphology.*
2. *Multi-headed microscopy*
3. *Use of blood or marrow photomicrographs with referee and consensus identifications (eg, former CAP surveys photomicrographs)*
4. *Use of digital images*
5. *Enrollment and participation of all personnel in an external assessment program for morphologic observation for peripheral blood smear morphology.*

In the case of comparative blood film WBC differentials, the method of Rümke is recommended to define statistical agreement among observers.

The laboratory director or designee must determine acceptability criteria for agreement. The laboratory must maintain records of performance and record corrective actions taken for personnel demonstrating significant discrepancies from the group consensus.

Evidence of Compliance:
- ✓ Records of evaluation **AND/OR**
- ✓ Records of enrollment/participation of staff in an external assessment program

HEM.34450 Slide Retention - CBC Differential **Phase I**

Blood film slides (peripheral blood smears) are retained for at least one week for possible review and/or reference.

NOTE: It may be desirable to retain outpatient films for a longer period and significantly abnormal films indefinitely for teaching purposes.

HEM.34500 Morphology Assessment **Phase II**

Personnel follow defined criteria to fully assess and accurately report WBC, RBC and platelet morphology as part of a manual WBC differential and/or blood film review.

NOTE: The laboratory must have a system to ensure that technical personnel have fully assessed all morphologic findings in each patient film. Each laboratory director should, in consultation with the medical staff, determine which morphologic findings are reportable. For example, minor degrees of anisocytosis and poikilocytosis without specific types of RBC abnormalities may be considered within the normal spectrum and not reportable to the chart. For RBC abnormalities that are reported, the laboratory must define a qualitative or semiquantitative grading system. When defined abnormalities (eg, spherocytes, target cells, fragments, etc.) are present, non-specific listings of "anisocytosis" and/or "poikilocytosis" may not provide additional clinically useful information.

Evidence of Compliance:
- ✓ Patient reports that show assessment and reporting of morphologic findings

HEM.34600 Criteria for Blood Film Review **Phase II**

The laboratory follows defined criteria for review of specified findings on blood films by the pathologist, supervisor, or other technologist qualified in hematomorphology.

Evidence of Compliance:
- ✓ Patient reports with reviewer comments **OR** electronic record **OR** review log

BLOOD FILMS FOR MICROORGANISMS

HEM.34655 Blood Film Microorganism Detection **Phase II**

Blood films submitted for microscopic examination allow for detection of microorganisms that may be present.

NOTE: Microorganisms that should be recognized, if present, include parasites, such as Plasmodium species, trypanosomes, and microfilaria. Occasionally, the morulae of Anaplasma and Ehrlichia, which are bacteria, may be seen. Spirochetes of the Borellia genus may be seen in patients with relapsing fever. Yeasts may sometimes be seen in patients with disseminated histoplasmosis or with fungemia caused by other yeast species (eg, Candida species or Malassezia species).

Evidence of Compliance:
- ✓ Blood parasitology atlas or reference materials

HEM.34687 Parasite Load Reporting **Phase I**

When blood films are positive for malaria parasites *(Plasmodium* spp.), the parasite load (provided as percentage parasitemia or the number of parasites per µL of blood) is reported along with the organism identification.

NOTE: It is important to determine the parasite load when blood films are reviewed and found to be positive for malaria parasites because this information may be used to guide treatment decisions and monitor the response to therapy. Due to the potential for drug resistance in some of the Plasmodium species, particularly P. falciparum, it is important that every positive smear be assessed and the parasite load reported exactly the same way on follow-up specimens as on the initial specimen. This allows the parasite load to be monitored after therapy has been initiated. The parasite load will usually drop very quickly within the first 24 hours; however, in cases of drug resistance, the level may not decrease, but actually increase over time.

Although there are currently no requirements for reporting parasite load when blood films are positive for Babesia species, physicians may ask for these data to guide treatment decisions and monitor the response to therapy.

Evidence of Compliance:
- ✓ Patient reports for positive malaria cases

HEM.34724 Thick and Thin Films **Phase II**

Both thick and thin films (routine blood films and/or buffy coat films), or methods of equivalent sensitivity, are made to provide thorough examination for blood parasites.

HEM.34798 Malaria Stain Buffer pH **Phase I**

There are records that malaria stains are washed with a buffer of a pH appropriate for the stain used.

NOTE: The ideal buffer pH for Plasmodium species identification is 7.0-7.2, as it allows for optimal visualization of malarial cytoplasmic inclusions (eg, Schüffner's dots and Maurer's clefts).

HEM.34872 Slide Review Procedure **Phase I**

An adequate number of fields is examined under the 100 X oil-immersion objective (eg, 300 fields).

AUTOMATED RETICULOCYTES

HEM.35150 Spurious Reticulocyte Results **Phase I**

The laboratory has a process to detect spurious automated reticulocyte results prior to reporting.

NOTE: Since all DNA- and RNA-containing cells will stain with DNA-RNA fluorescent dyes, the process must identify when the instrument cannot discriminate such stained particles from true reticulocytes. Potential interferences include Howell-Jolly bodies, nucleated erythrocytes, Heinz bodies, basophilic stippling of red cells, macrothrombocytes, megakaryocyte fragments, platelet clumps, and malaria or other intracellular organisms. Erythrocyte agglutination also may give spuriously high results, as may very high leukocytosis or thrombocytosis. Interfering particles may vary, depending on instrumentation, dye, and reaction conditions. Based upon initial evaluation of the instrument by the laboratory, criteria must be developed to detect samples with potentially erroneous results. This may be accomplished through flagging algorithms incorporated in the instrument and by examination of a blood film from every sample to ensure absence of relevant interferences.

Evidence of Compliance:

- ✓ Records showing actions taken to verify reticulocyte count prior to reporting

MANUAL RETICULOCYTES

HEM.35250 Reticulocyte Blood Film Quality **Phase I**

The quality of reticulocyte blood films is satisfactory (properly stained, free of precipitate, good cell distribution).

HEM.35300 Reticulocyte Concentration **Phase I**

The reported reticulocyte concentration is based on a minimum sample size of 1,000 RBC.

NOTE: The written procedure must describe the method, number of cells counted, and calculations used.

Commercial controls are not necessary for manual reticulocyte counts.

BODY FLUIDS

MANUAL CELL COUNT - BODY FLUID

HEM.35319 Diluting Equipment **Phase II**

Certified pipettes or commercial dilution systems are used when diluting body fluid samples.

HEM.35338 Background Checks - Manual Counts **Phase II**

The diluting fluid is checked for interfering background particulates and changed when indicated.

NOTE: Checking can be done by examining samples of these fluids under the microscope. The check must be performed each day of use for manual diluting methods. If commercial microdilution systems are used, daily checks are not required but each lot must be examined visually for uniformity of filling and clarity. If diluting fluids are prepared by the laboratory, they must be prepared aseptically; refrigeration is recommended to prevent contamination with microorganisms.

Evidence of Compliance:
- ✓ Records of background checks

HEM.35340 Manual Cell Count Controls **Phase II**

For manual body fluid cell counts, the laboratory analyzes at least one cell count control specimen in duplicate or uses a procedural control each eight hours of patient testing.

NOTE: This requirement can be met with assayed liquid control material, a previously assayed patient sample, or a procedural control. An example of a procedural control is correlation of the cell count with the cellularity of a stained slide prepared by a standard, validated method. Liquid control materials must be tested in duplicate.

Evidence of Compliance:
- ✓ Records of cell count or procedural controls at defined frequency

HEM.35347 Counting Chamber and Optical Grid Quality **Phase I**

The lines in all counting or motility chambers, ocular micrometers, and optical grids are bright and free from scratches, dirt, or debris.

HEM.35357 Body Fluid Analysis Procedure **Phase II**

For manual body fluid cell counts, each sample is counted in duplicate.

NOTE: Testing records must reflect the performance of the counts in duplicate for all counting chambers. Limits of agreement between replicate counts must be defined.

Evidence of Compliance:
- ✓ Records or worksheets reflecting duplicate counts and corrective action when limits of agreement are exceeded

HEM.35376 Cell Clumps/Debris - Manual Methods **Phase II**

The laboratory indicates (as part of the report) that results may be inaccurate if the fluid specimen is partially clotted or has cell clumps or debris on the counting chamber.

HEM.35395 Red Cell Confirmation Techniques **Phase I**

There is an additional procedure beyond unstained bright-field microscopic visualization of cells on the hemocytometer used when necessary to ensure the accurate distinction of erythrocytes from other cell types.

NOTE: Suggested techniques include acid rinsing of the fluid sample to lyse erythrocytes after initially counting all cells, the addition of a stain such as methylene blue to improve recognition of non-erythrocytes, correlation with the number and proportion of cells on the cytospin preparation or phase microscopy.

Evidence of Compliance:
- ✓ Records of confirmation testing

NUCLEATED CELL DIFFERENTIALS - BODY FLUID

HEM.35528 Body Fluid Cell Differentials **Phase I**

The method for differentiating body fluid cells is appropriate for the intended clinical use.

NOTE: The laboratory should use stained cytocentrifuge preparations to facilitate quantitative differentials and complete classification of nucleated cell types in body fluids, as opposed to performing differentials of unstained hemocytometer preparations. Differentials based on supravitally-stained hemocytometer preparations, wedge smears and drop preparations are considered suboptimal; their use should be limited to clinical circumstances requiring differentiation of polymorphonuclear from mononuclear cells (eg, bacterial meningitis). Further sub-classification of nucleated cells, particularly the detection of malignant cells, should be performed using slide preparation methods that provide optimal cell recovery and morphologic detail, such as cytocentrifugation. Cytocentrifuge preparations provide excellent morphologic detail, deliver a high yield of cells even when the concentration is low, and have a high rate of detection for malignant cells. In cases of leukemia or lymphoma, Romanowsky-stained cytospin slides show excellent morphologic correlation with blood and bone marrow smears. If the laboratory uses an alternate slide preparation method or stain for sub-classification of body fluid mononuclear cells and/or detection of malignant cells, it must demonstrate from literature or in-house studies that this technique is equivalent in cell yield/recovery and morphologic detail to Romanowsky-stained cytocentrifuge preparations.

Evidence of Compliance:
- ✓ Records showing in-house or literature validation of techniques other than Romanowsky-stained cytocentrifuge preparations

HEM.35547 Body Fluid Smear Quality **Phase I**

The quality of body fluid smears is satisfactory (uniform cell distribution, appropriate dilution so cells are not crowded, properly stained, adequate cell yield, ready recognition of cell types that are reported).

HEM.35566 Morphologic Observation Evaluation - Body Fluid **Phase II**

The laboratory evaluates consistency of morphologic observation among personnel performing body fluid cell differentials at least annually.

NOTE: The laboratory must ensure the identification of body fluid cells is reported consistently amongst all personnel performing the microscopic analysis.

Suggested methods to accomplish this include:
1. *Circulation of a pre-graded set of body fluid smears with defined nucleated cell differential distributions*
2. *Multi-headed microscopy*
3. *Use of body fluid photomicrographs with referee and consensus identifications (eg, former CAP Surveys photomicrographs)*
4. *Use of digital images*
5. *Enrollment and participation of all personnel in an external assessment program for morphologic observation for body fluid differentials.*

The laboratory director or designee must determine acceptability criteria for agreement. The laboratory must maintain records of performance and record corrective actions taken for personnel demonstrating significant discrepancies from the group consensus.

Evidence of Compliance:
- ✓ Records of evaluation **AND/OR**
- ✓ Records of enrollment/participation of staff in an external assessment program

HEM.35585 Slide Review **Phase II**

Slides with suspected malignant cells are reviewed by a pathologist or other qualified physician before final results reporting.

Evidence of Compliance:
- ✓ Records of slide review

HEM.35604 Microscopic Result Comparison **Phase I**

If a body fluid specimen has a microscopic examination in more than one area of the laboratory, there is a mechanism to compare the data and interpretations from these different areas when a diagnosis of malignancy is suspected.

Evidence of Compliance:
- ✓ Records of comparison

HEM.35623 Cytomorphology Reference Library **Phase I**

There is a file of unusual slides and/or an atlas of body fluid cytomorphology readily available to the technologist evaluating the slides, to assist in the identification of cell types.

HEM.35642 Slide Retention - Body Fluid Differential **Phase I**

Body fluid slides (eg, pleural fluid, seminal fluid) are retained for at least one week for possible review and/or reference.

NOTE: The laboratory may choose to retain significantly abnormal smears (eg, those demonstrating microorganisms, cytologically suspicious or overtly malignant cells, etc.) for longer periods to allow for review as part of the laboratory's correlative or quality assurance programs or delayed clinical queries, as defined in the laboratory's slide retention policy. If a longer retention period is defined, it must be followed.

RESULT REPORTING - BODY FLUID

HEM.35650 Body Fluid Result Reporting of Nucleated Cells **Phase I**

When absolute total cell counting methods cannot reliably distinguish white blood cells from other nucleated cells, body fluid cell counts and differential results are reported with the total nucleated cell count and a differential with all nucleated cell types observed.

NOTE: If the absolute total cell counting method in the laboratory cannot reliably distinguish white blood cells from other nucleated cells (eg, unstained bright-field visualization of cells in a hemocytometer chamber and certain automated counting technologies), the laboratory must report the absolute total cell count (cells/µL) as TNC (total nucleated cells) not WBC (total white blood cells). The relative differential (% of total cells counted) performed on a stained

cytocentrifuge slide, which can reliably distinguish white blood cells from other nucleated cells, must include the percentage of all nucleated cell types (eg, lymphocyte, neutrophil, monocyte/ macrophage, basophils, eosinophil, plasma cell, mesothelial cell, bronchial lining cell, synovial lining cell, ventricular lining cell, endothelial cell, squamous epithelial, and other) when TNC is reported for the absolute total cell count.

Evidence of Compliance:

- ✓ Patient report with body fluid cell count and differential results

ABNORMAL HEMOGLOBIN DETECTION

For purposes of diagnosing hemoglobinopathies, more than one test may be necessary. As an example, hemoglobin solubility testing alone is not sufficient for detecting or confirming the presence of sickling hemoglobins in all situations.

HEM.35925 Hb S Primary Screen **Phase II**

For patient samples that appear to have Hb S in the primary screening by electrophoresis or other separation methods, the laboratory either: 1) performs a second procedure (solubility testing, or other acceptable method) to confirm the presence of Hb S, or 2) includes a comment in the patient report recommending that confirmatory testing be performed.

NOTE: For primary definitive diagnosis screening by electrophoresis or other separation methods, all samples with hemoglobins migrating in the "S" positions or peak must be tested for solubility or by other acceptable confirmatory testing for sickling hemoglobin(s). Known sickling and non-sickling controls both must be included with each run of patient specimens tested.

RESULTS REPORTING - HEMATOLOGY

*****REVISED** 12/26/2024***

HEM.36820 Reference Intervals **Phase II**

Patient results are reported with accompanying reference intervals or interpretive ranges.

NOTE: For WBC differential counts, the CAP recommends that laboratories report absolute cell counts, along with their corresponding reference intervals. The CAP discourages the reporting of percent cell counts without absolute counts on WBC differentials. Laboratories reporting only percent cell counts must provide laboratory established reference intervals.

Under some circumstances it may be appropriate to distribute lists or tables of reference intervals (printed copies or electronic data) to users and sites where reports are received. The laboratory must ensure that such data is up to date.

Reference interval citations from the manufacturer's insert or published literature citations may be used to determine the reference interval. However, reference intervals have not been published for many body fluid analytes and obtaining normal fluids to establish reference intervals may not be feasible. If reference intervals are not available, results must be accompanied by an appropriate comment such as, "The reference interval(s) and other method performance specifications are unavailable for this body fluid. Comparison of the result with concentration in the blood, serum, or plasma is recommended."

Evidence of Compliance:
✓ Patient reports

COAGULATION

SPECIMEN COLLECTION AND HANDLING - COAGULATION

HEM.36840 Specimen Collection - Intravenous Lines **Phase I**

Instructions for the clearing (flushing) of intravenous lines before drawing specimens for hemostasis testing are defined and followed.

NOTE: Collection of blood for coagulation testing through intravenous lines that have been previously flushed with heparin should be avoided, if possible. If the blood must be drawn through an indwelling catheter, possible heparin contamination and specimen dilution must be considered. When obtaining specimens from indwelling lines that may contain heparin, the line should be flushed with 5 mL of saline, and the first 5 mL of blood or 6-times the line volume (dead space volume of the catheter) be drawn off and not used for coagulation testing. For those specimens collected from a normal saline lock (capped off venous port) twice the dead space volume of the catheter and extension set should be discarded.

HEM.36860 Anticoagulant - Coagulation **Phase I**

Routine coagulation specimens are collected into 3.2% buffered sodium citrate.

NOTE: Sodium citrate is effective as an anticoagulant due to its mild calcium-chelating properties. Of the 2 commercially available forms of citrate, 3.2% buffered sodium citrate (105-109 mmol/L of the dihydrate form of trisodium citrate $Na_3C_6H_5O_7 \cdot 2H_2O$) is the recommended anticoagulant for coagulation testing. Reference intervals for clot-based assays must be determined using the same concentration of sodium citrate that the laboratory uses for patient testing. The higher citrate concentration in 3.8% sodium citrate, may result in falsely lengthened clotting times (more so than 3.2% sodium citrate) for calcium-dependent coagulation tests (ie, PT and aPTT) performed on slightly underfilled samples and samples with high hematocrits. The prolonged results are also more pronounced when the clotting time is abnormal, such as in samples from patients on warfarin therapy. Both the World Health Organization and CLSI recommend utilizing 3.2% sodium citrate (105-109 nm/L), as the thromboplastin International Sensitivity Index (ISI) values applied in the INR calculations are based on specimens collected in 3.2% sodium citrate. Coagulation testing cannot be performed in samples collected in EDTA due to the more potent calcium chelation. While certain assay systems, such as platelet mapping via thromboelastography require heparin, heparinized tubes are not appropriate for clot-based plasma assays due to the inhibitory effect of heparin on multiple coagulation proteins. Other testing for platelet function, such as light transmission platelet aggregation assay can be performed on 3.2% or 3.8% sodium citrate.

*****REVISED** 12/26/2024***
HEM.36880 Fill Volume and Specimen Mixing - Coagulation **Phase I**

Instructions for the acceptable fill volume and mixing of specimen collection tubes for coagulation testing are defined and followed.

NOTE: The recommended proportion of blood to the sodium citrate anticoagulant volume is 9:1. Inadequate filling of the collection device will decrease this ratio, and may lead to inaccurate

results for calcium-dependent clotting tests, such as the PT and aPTT. The effect on clotting time from under-filled tubes is more pronounced when samples are collected in 3.8% rather than 3.2% sodium citrate. The effect of fill volume on coagulation results also depends on the reagent used for testing, size of the evacuated collection tube, and citrate concentration. A minimum of 90% fill is recommended; testing on samples with less than 90% fill should be validated by the laboratory. It is unacceptable to combine the contents from separate, underfilled sodium citrate collection tubes.

Samples should be gently inverted to prevent clotting, in keeping with the manufacturer's instructions and laboratory's specimen collection instructions as described in GEN.40100.

Evidence of Compliance:

✓ Records of rejected specimens

HEM.36900 Elevated Hematocrits - Coagulation **Phase I**

Instructions for the detection and special handling of specimens with elevated hematocrits are defined and followed.

NOTE: A hematocrit value >55% may lead to spurious coagulation results. The citrate anticoagulant distributes only in the plasma and not into the blood cells. For this reason, plasma citrate concentration will be increased if the patient's hematocrit is greater than 55%, potentially leading to spuriously prolonged PT and aPTT results, as well as erroneous results for other calcium-dependent clotting tests such as clottable protein C/protein S and factor assays.

If possible, a new phlebotomy should be performed, using a reduced volume of sodium citrate, adjusted for the elevated hematocrit. Conversely, there are no current data to support a recommendation for adjusting the citrate concentration in the presence of severe anemia (hematocrit <20%).

*****REVISED** 08/24/2023***

HEM.36920 Specimen Quality Assessment - Coagulation **Phase II**

Coagulation specimens are checked for clots before reporting results.

NOTE: Specimens with grossly visible clots may have extremely low levels of fibrinogen and variably decreased levels of other coagulation proteins, causing PT, aPTT, fibrinogen and other coagulation assays results to be inaccurate or unobtainable. Checking for clots may be done before or after testing:

- *With applicator sticks, where appropriate (should not be used with viscoelastic testing)*
- *By visual inspection of whole blood samples for large clots or centrifuged plasma for small clots*
- *By analysis of results including waveform analysis or delta checks as applicable*

Laboratories receiving centrifuged specimens (eg, frozen plasma) cannot rely on visual inspection alone to detect specimen quality issues. For example, if a clot is not detected during PT and aPTT testing and the fibrinogen level is <25 mg/dL, the sample may actually be serum instead of plasma.

The laboratory must have a mechanism to identify these specimens appropriately and/or to reject specimens, as applicable. Laboratories must work with their clients that perform specimen processing to ensure that they practice appropriate specimen handling for coagulation specimens.

Evidence of Compliance:

✓ Records of rejection for clotted specimens

HEM.36940 Specimen Handling for Plasma-based Testing - Coagulation **Phase II**

Coagulation tests are promptly performed on fresh plasma, or the platelet-poor plasma is frozen until testing can be performed.

NOTE: After blood collection, there is progressive degradation of the labile coagulation factors V and VIII, leading to increasing prolongation of the aPTT and PT. The allowable time interval between specimen collection and sample testing depends on the temperature encountered during transport and storage of the specimen. Allowable time intervals are as follows:

1. *PT specimens, uncentrifuged or centrifuged with plasma remaining in the capped tube above the packed cells, or as centrifuged plasma separated from the cells, should be kept at room temperature (18 to 24°C) and tested no longer than 24 hours from the time of specimen collection. PT specimens should not be refrigerated (during storage).*
2. *aPTT specimens, uncentrifuged or centrifuged with plasma remaining in the capped tube above the packed cells, should be kept at room temperature (18 to 24°C) and tested no longer than 4 hours after the time of specimen collection.*
3. *aPTT specimens that are centrifuged and plasma separated from cells can be kept for 4 hours refrigerated (2 to 8°C) or at room temperature (18 to 24°C). Samples for unfractionated heparin testing should be centrifuged within one hour from the time of specimen collection*
4. *Samples for other coagulation factors (eg, thrombin time, protein C, factor V, factor VIII) have variable stability and should be kept in the same manner as aPTT samples*

If PT or aPTT testing cannot be performed within these times, platelet-poor plasma should be removed from the cells and frozen at –20°C for up to 2 weeks or at –70°C for up to 12 months. If a laboratory has established an allowable time interval different than that detailed above, data must be available to verify that coagulation testing is valid in the time interval established.

***NEW** 12/26/2024*

HEM.36960 Specimen Handling for Whole Blood-Based Testing - Coagulation **Phase II**

Specimens for whole blood-based coagulation testing are handled according to manufacturer's instructions or as validated by the laboratory.

NOTE: Specimens must not be:

- *Heated, refrigerated, or frozen*
- *Centrifuged - Centrifuged specimens must be rejected. Reconstitution of a centrifuged specimen by mixing is not adequate.*

For additional specimen handling for platelet function studies, refer to HEM.38350.

HEM.37150 DIC - Test Availability **Phase II**

Tests for defining or monitoring disseminated intravascular coagulation (DIC) are available, if applicable to the patient population served.

NOTE: At a minimum, the platelet count, aPTT, PT/INR, fibrinogen assay and D-dimer (or FDP) must be available.

Laboratories may wish to refer to criteria published by the International Society on Thrombosis and Haemostasis (ISTH) and the Japanese Ministry of Health and Welfare for further information.

***REVISED** 08/24/2023*

HEM.37165 Coagulation Testing and Therapeutic Anticoagulant Recommendations **Phase I**

Recommendations are available to clinicians on the following:

- **Laboratory tests used for monitoring heparin, low molecular weight heparin, direct thrombin inhibitors (eg, lepirudin, bivalirudin, argatroban) and/or oral anticoagulant therapy**
- **Utility and limitations of viscoelastic testing**

- **The therapeutic range for the tests, if available**
- **Information about potential interferences of anticoagulant medications on coagulation testing.**

NOTE: The coagulation tests available to clinicians should be applicable to the anticoagulant drugs in use, and information is available on the test values that indicate that the anticoagulant is present and/or is in a therapeutic range, when available.

For vitamin K antagonists (eg, warfarin), the prothrombin time (PT/INR) is recommended. Direct oral anticoagulant medications (non-vitamin K) should not be monitored with PT/INR or aPTT because the effect of these tests is not predictable. For unfractionated heparin the activated partial thromboplastin time (aPTT) and/or activated clotting time are commonly used, but the heparin assay (factor Xa inhibition) may also be employed. For low molecular weight heparin or danaparoid, monitoring is often not necessary, but the heparin assay (Xa inhibition assay) may be used in certain circumstances, as the aPTT is generally insensitive to the effect of these agents. Direct parenteral thrombin inhibitors are often monitored using the aPTT. The thrombin time may be useful to qualitatively verify the presence of direct thrombin inhibitors.

For viscoelastic testing, recommendations on the utility of testing in clinically meaningful situations must be available, including the following as applicable:

- *Proper test selection*
- *Instrument comparability and/or*
- *Recommendations for viscoelastic testing-based monitoring of antiplatelet or anticoagulant medications.*

Evidence of Compliance:

✓ Memoranda to physicians, test reference guide, interpretive comments in patient reports, or other mechanism for providing recommendations to physicians for ordering and interpreting coagulation tests used for diagnostic purposes and anticoagulant therapy monitoring

HEM.37175 Platelet-poor Plasma **Phase I**

At least annually and after major centrifuge maintenance or service, the laboratory measures the actual platelet count of the "platelet-poor" plasma used for many coagulation tests.

NOTE: Platelet-poor plasma is particularly important when testing for the presence of a lupus anticoagulant, when measuring the level of unfractionated heparin, and in plasma samples to be frozen for later testing. Platelet-poor plasma should have a residual platelet concentration of less than 10 X 10^9/L. This is important because platelet membranes form a procoagulant surface that can accelerate coagulation and spuriously shorten clotting times. It is particularly important when testing for the presence of a lupus anticoagulant; due to the high content of lipid in the platelet plasma membrane, increased platelets in samples with the lupus anticoagulant can cause the antiphospholipid antibody to bind to the platelet membrane, thus effectively removing it from plasma. In this circumstance, the presence of lupus anticoagulant may not be detected during diagnostic testing. Use of a 0.2-µm filter to achieve platelet-poor plasma samples is not appropriate for all plasma-based coagulation studies. Filtration of plasma can result in selective removal of factors V, VIII, IX, XII, and vWF; thus filtration of plasma to achieve a platelet-poor specimen is discouraged. aPTT, prothrombin time/international normalized ratio (PT/NR) and thrombin clotting time (TT) performed on fresh plasma samples are not affected by platelet counts of at least up to 200 x 10^9/L (200,000/µL).

Samples to be frozen should be "platelet-poor" because plasma contaminated with significant numbers of platelets may yield different analytic results after thawing, due to lysis of platelets.

Evidence of Compliance:

✓ Records of platelet concentration checks on all centrifuges used to prepare platelet-poor plasma

QUALITY CONTROL - COAGULATION

HEM.37300 Coagulation Quality Control **Phase II**

The laboratory performs controls using two different levels of control material each eight hours of patient testing and each time there is a change in reagents, or more frequently if specified in manufacturer's instructions, laboratory procedure, or the CAP Checklist.

*NOTE: **This includes photo-optical, electromechanical and manual methods.***

For manual methods (ie, tilt tube method), controls must be performed by each individual who performs the tilt tube test in the same eight hour period.

If an internal quality control process (eg, electronic/procedural/built-in) is used instead of an external control material to meet daily quality control requirements, the laboratory must have an individualized quality control plan (IQCP) approved by the laboratory director defining the control process, including the frequency and use of external and internal controls. At a minimum, external control materials must be analyzed with new lots and shipments of reagents or more frequently if indicated in the manufacturer's instructions. Please refer to the IQCP section of the All Common Checklist for the eligibility of tests for IQCP and requirements for implementation and ongoing monitoring of an IQCP.

Evidence of Compliance:

- ✓ Records of QC results including external and internal control processes **AND**
- ✓ Manufacturer product insert or manual

COAGULATION TESTS BASED ON DIRECT MEASUREMENT OF ANALYTES

CAP accredited chemistry laboratories have been applying the concepts and procedures for calibration, calibration verification, and analytic measurement range (AMR) verification to calibrated analytical methods for many years. Section directors and technologists with chemistry backgrounds will be helpful consultants to their coagulation laboratory colleagues as calibration verification and AMR verification requirements evolve.

The checklist requirements apply to hemostasis test methods that are calibrated and directly measure the concentration or activity of an analyte by employing enzyme immunoassay (EIA), including ELISA and fluorescence immunoassay, immunoturbidity and chromogenic methods. Examples of commonly performed hemostasis tests affected by these checklist requirements include: calibrated EIA or immunoturbidity methods for coagulation factors, protein C antigen, free and total protein S antigens, von Willebrand factor antigen, von Willebrand collagen binding activity, and quantitative D-dimer, and calibrated chromogenic assays for antithrombin activity, protein C activity, and heparin or low molecular weight heparin. This list is not exhaustive, and laboratory directors should review their laboratory's test menu to identify additional tests which fall into the categories of methodologies described above.

Clot-based methods, (including PT, aPTT, thrombin time, factor assays and fibrinogen, lupus anticoagulant, activated protein C resistance, qualitative and semi-quantitative assays) and all platelet function assays, including ristocetin cofactor activity are exempt.

CALIBRATION: The process of adjusting an instrument or test system to establish a relationship between the measurement response and the concentration or amount of the analyte that is being measured by the test procedure.

CALIBRATION VERIFICATION: The process of confirming that the current calibration settings for each analyte remain valid for a test system.

Each laboratory must define limits for accepting or rejecting results of the calibration verification process. Calibration verification can be accomplished in several ways. If the manufacturer provides a calibration validation or verification process, it must be followed. Other techniques include (1) assay of the current calibration materials as unknown specimens and (2) assay of matrix-appropriate materials with target values that are specific for the test system.

ANALYTICAL MEASUREMENT RANGE (AMR): The range of analyte values that a method can directly measure on the specimen without any dilution, concentration, or other pretreatment that is not part of the usual assay process.

LINEARITY AND THE AMR
Linearity is a fundamental characteristic of many analytic measurement methods, whereby there is a straight-line relationship between "true" analyte concentrations and measured concentrations. In this context, linearity refers to the relationship between the predicted and observed measurement results and not to the relationship between instrument signal output and analyte concentration. For most assays, this relationship is linear within the AMR.

AMR VERIFICATION
Laboratories are required to verify that the appropriate relationship is maintained over the AMR. Laboratories may verify and use an AMR that is narrower than the range defined by the manufacturer. This may be appropriate when materials available for method validation and/or AMR verification are not available to verify the full range claimed by the manufacturer, or reporting values across the full range defined by the manufacturer is not clinically relevant. For many assays, results beyond the AMR can be reported through dilution or concentration studies (see HEM.37380 & HEM.37385). AMR verification is not required for calculated test results (refer to the Definition of Terms in the All Common Checklist) as long as the individual results contributing to the calculation have AMR verification.

Minimum requirements for AMR verification can be met by using matrix appropriate materials, which include low, mid and high concentration or activity range of the AMR with recovery of results that fall within a defined range of the target value. Records of the AMR verification process must be available.

CLOSENESS OF SAMPLE CONCENTRATIONS OR ACTIVITIES TO THE UPPER AND LOWER LIMITS OF THE AMR
When verifying the AMR, it is required that samples tested are near the upper and lower limits of the AMR. Factors to consider in verifying the AMR are the expected analytic imprecision near the limits, the clinical impact of errors near the limits, and the availability of test specimens near the limits. It may be difficult to obtain specimens with values near the limits for some analytes. In such cases, reasonable procedures should be adopted based on available specimen materials. The closeness of sample concentrations or activities to the upper and lower limits of the AMR are defined at the laboratory director's discretion. The method manufacturer's instructions for verifying the AMR must be followed, when available. The laboratory director must define limits for accepting or rejecting tests of the AMR.

HEM.37360 Calibration Procedure **Phase II**

The laboratory calibrates each test system as defined and reviews the calibration records for acceptability.

NOTE: Calibration of FDA-cleared/approved methods must be performed following the manufacturer's instructions, at minimum, including the number, type, and concentration of calibration materials, frequency of calibration, and criteria for acceptable performance. Calibration procedures are typically specified in the manufacturer's instructions but may also be established by the laboratory.

HEM.37363 Calibration and Calibration Verification Materials **Phase II**

High quality materials with test system and matrix-appropriate target values are used for calibration and calibration verification whenever possible.

NOTE: Calibration and calibration verification must have defined analyte target values and appropriate matrix characteristics for the clinical specimens and specific assay method. Many instrument systems require calibration materials with system-specific target values to produce accurate results for clinical specimens.

Suitable materials for calibration verification include, but are not limited to:

1. *Calibrators used to calibrate the analytical system*
2. *Materials provided by the manufacturer for the purpose of calibration verification*
3. *Previously tested unaltered patient/client specimens*
4. *Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method*
5. *Third party general purpose reference materials that are suitable for verification*

In general, routine control materials and proficiency testing materials are not suitable for calibration verification, except in situations where the material has been shown to be suitable (eg, specifically designated by the method manufacturer) or no other materials are available.

Evidence of Compliance

✓ Records of calibration and calibration verification

HEM.37365 Recalibration/Calibration Verification Criteria **Phase II**

Criteria for the frequency and acceptability of recalibration or calibration verification are defined and followed.

NOTE: Laboratories must either recalibrate or perform calibration verification at least every six months and if any of the following occur:

1. *At changes of reagent lots unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client results*
2. *If QC shows an unusual trend or shift or is outside acceptable limits, and the system cannot be corrected to bring control values into the acceptable range*
3. *After major preventive maintenance or change of critical instrument component*
4. *When recommended by the manufacturer*

Single use devices, and other test devices that do not allow user calibration, do not require calibration verification.

Evidence of Compliance:

✓ Records of calibration verification at defined frequency

HEM.37370 Recalibration **Phase II**

The test system is recalibrated when calibration verification fails to meet the established criteria of the laboratory.

Evidence of Compliance:

✓ Records of recalibration, if calibration or calibration verification has failed

*****REVISED** 08/24/2023***

HEM.37373 AMR Verification Materials **Phase II**

Verification of the analytical measurement range (AMR) is performed with matrix-appropriate materials, which, at a minimum, include the low, mid and high range of the AMR, and appropriate acceptance criteria are defined.

NOTE: The matrix of the sample (ie, the environment in which the sample is suspended or dissolved) may influence the measurement of the analyte. In many cases, the method manufacturer will recommend suitable materials. Other suitable materials for AMR verification include the following:

1. *Linearity material of appropriate matrix, eg, CAP CVL Survey-based or other suitable linearity verification material*
2. *Previously tested patient/client specimens, that may be altered by admixture with other specimens, dilution, spiking in known amounts of an analyte, or other technique*
3. *Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method*
4. *Patient samples that have reference method assigned target values*
5. *Control materials, if they adequately span the AMR and have method specific target values*

Factors to consider in verifying the AMR are the expected analytic imprecision near the limits, the clinical impact of errors near the limits, and the availability of test specimens near the limits. It may be difficult to obtain specimens with values near the limits for some analytes. In such cases, reasonable procedures should be adopted based on available specimen materials. The closeness of sample concentrations and activities to the upper and lower limits of the AMR are defined at the laboratory director's discretion.

Evidence of Compliance:

✓ Records of AMR verification

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HEM.37375 AMR Verification **Phase II**

Verification of the analytical measurement range (AMR) is performed at least every six months and following the defined criteria. Records are retained.

NOTE: The AMR must be verified at least every six months after a method is placed in service and if any of the following occur:

1. *A change of reagent lots unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client results, and the range used to report patient/client test data.*
2. *If QC shows an unusual trend or shift or is outside acceptable limits, and the system cannot be corrected to bring control values into the acceptable range*
3. *After major preventive maintenance or change of a critical instrument component*
4. *When recommended by the manufacturer*

It is not necessary to independently verify the AMR if the calibration of an assay includes calibrators that span the full range of the AMR, with low, midpoint and high values represented (ie, three points) and if the system is calibrated at least every six months. A one-point or two-point calibration does not include all of the necessary points to verify the AMR.

AMR verification is not required for clot-based coagulation tests, platelet function tests, and other tests where output is a unit of time or arbitrary reporting unit (rather than measured analyte concentration). AMR verification is not required for calculated test results as long as the individual results contributing to the calculation have AMR verification.

Evidence of Compliance:

✓ Records of AMR verification, as required, at least every six months

HEM.37380 Diluted or Concentrated Samples **Phase II**

If a result is greater than or less than the AMR, a numeric result is not reported unless the sample is processed by dilution, a mixing procedure or concentration so that the processed result falls within the AMR.

NOTE:

1. *A measured value that is outside the AMR may be unreliable and should not be reported in routine practice. Dilution, a mixing procedure* or concentration of a sample may be required to achieve a measured analyte activity or concentration that falls within the AMR. The processed result must be within the AMR before it is mathematically corrected by the concentration or dilution factor to obtain a reportable numeric result.*
2. *For each analyte, the composition of the diluent solution and the appropriate volumes of sample and diluent must be specified in the procedure manual. Specifying acceptable volumes is intended to ensure that the volumes pipetted are large enough to be accurate without introducing errors in the dilution ratio.*
3. *All dilutions, whether automatic or manual, should be performed in a way that ensures that the diluted specimen reacts similarly to the original specimen in the assay system. For some analytes, demonstrating that more than one dilution ratio similarly recovers the elevated concentration may be helpful.*
4. *This checklist requirement does not apply if the concentration or activity of the analyte that is outside the AMR is reported as "greater than" or " less than" the limits of the AMR.*

**This procedure is termed the "method of standard additions." In this procedure, a known quantity (such as a control) is mixed with the unknown, and the concentration of the mixture is measured. If equal volumes of the two samples are used, then the result is multiplied by two, the concentration of the known subtracted, and the concentration of the unknown is the difference.*

Evidence of Compliance:

✓ Patient reports or worksheets

HEM.37385 Maximum Dilution **Phase II**

For analytes that may have results falling outside the limits of the AMR, the laboratory defines the maximum dilution that may be performed to obtain a reportable numeric result.

NOTE:

1. *For each analyte, the laboratory protocol should define the maximum dilution that falls within the AMR and that can be subsequently corrected by the dilution factor to obtain a reportable numeric result. Note that for some analytes, an acceptable dilution protocol may not exist because dilution would alter the analyte or the matrix causing erroneous results. Also note that, for some analytes, there may be no clinical relevance to reporting a numeric result greater than a stated value.*
2. *Analytes for which a dilution protocol is unable to bring the activity or concentration into the AMR should be reported as "greater than" the highest estimated values.*
3. *Establishment of allowable dilutions is performed when a method is first placed into service and is reviewed biennially thereafter as part of the procedure manual review by the Laboratory Director or designee. The laboratory director is responsible for establishing the maximum allowable dilution of samples that will yield a credible laboratory result for clinical use.*

Evidence of Compliance:

✓ Patient reports or worksheets

HEM.37390 Cut-Off Values for Qualitative Tests **Phase II**

For qualitative tests that use a quantitative cut-off value to distinguish positive from negative results, the analytic performance around the cut-off value is verified or established initially, and reverified at least every six months thereafter.

NOTE: This requirement applies to tests that report qualitative results based on a quantitative measurement using a threshold (cut-off value) to discriminate between positive and negative results for clinical interpretation. It does not apply to methods where the laboratory is not able to access the actual numerical value from the instrument.

Appropriate materials for establishment and verification of the cut-off are identical to those recommended for calibration verification. The requirement can be satisfied by the process of calibration or calibration verification using calibrators or calibration verification materials with values near the cut-off. It may also be satisfied by the use of QC materials that are near the cut-off value if those materials are claimed by the method manufacturer to be suitable for verification of the method's calibration process.

Verification of the cut-off should also be performed at changes of lots of analytically critical reagents (unless the laboratory director has determined that such changes do not affect the cut-off), after replacement of major instrument components, after major service to the instrument, and when QC materials reflect an unusual trend or shift or are outside of the laboratory's acceptable limits, and other means of assessing and correcting unacceptable control values fail to identify and correct the problem.

For FDA-cleared or approved tests, the clinical appropriateness of the cut-off value is evaluated as part of the clinical validation performed by the manufacturer. For laboratory-developed tests and modified FDA-cleared or approved tests, refer to COM.40640 for validation of clinical claims.

Evidence of Compliance:

- ✓ Records of initial establishment and verification of the cut-off value at defined frequency

COAGULATION STUDIES

PT/INR AND APTT

HEM.37400 Alternative Method Criteria **Phase I**

For photo-optical coagulation systems, the laboratory defines and follows criteria for determining when alternative procedures are performed (eg, lipemia, hyperbilirubinemia, turbidity, etc.).

NOTE: Very long clotting times may not be reproducible on an automated coagulation instrument. Criteria must be established by each laboratory for performance of the PT or aPTT by an alternate technique (eg, manual method) when the readable range of the instrument is exceeded. In addition, criteria must be provided for performance of alternate procedures in the presence of significant hyperbilirubinemia or lipemia, paradoxically short aPTTs and non-duplicating aPTTs.

Evidence of Compliance:

- ✓ Records showing results from alternative procedures, as applicable

HEM.37600 Clot Detection **Phase II**

For electromechanical coagulation systems with reusable probes to detect a clot, instructions for cleaning the probes are available.

HEM.37800 Duplicate Testing - Manual Testing **Phase II**

Manual coagulation testing (eg, PT, aPTT, fibrinogen) determinations are performed in duplicate and criteria for agreement are defined.

Evidence of Compliance:

- ✓ Records or worksheets reflecting duplicate testing of each sample including corrective action when limits of agreement are exceeded

HEM.37820 ISI **Phase II**

The ISI is appropriate to the particular PT reagent and instrumentation used.

NOTE: The laboratory must demonstrate appropriateness of its ISI, a measurement of the sensitivity with which thromboplastin reagents detect decreased levels of vitamin K-dependent coagulation factors. The ISI used must be appropriate for the particular reagent-instrument combination and method of clot detection. Acceptable records include information from the instrument/reagent manufacturer or local calibration using an FDA-approved product. This is especially true for photo-optical vs. electromechanical instruments, but may also vary among different instruments within the same classification.

Evidence of Compliance:

- ✓ Record showing information from the instrument/reagent manufacturer **OR** use of an ISI calculated from laboratory specimens

HEM.37830 INR Calculation Adjustment for ISI **Phase II**

The calculation of the INR is adjusted using the appropriate ISI value for every new lot of PT reagent, changes in types of reagent, or change in instrumentation.

NOTE: The ISI value usually changes with each new lot of PT reagent. The ISI reflects the sensitivity of the PT reagent to decreased levels of the vitamin K-dependent coagulation factors. This change in sensitivity will affect the calculation of the INR value.

The laboratory must be able to provide records that calculation of the INR is correct and that the ISI value is appropriate for the lot of thromboplastin reagent and for the method of clot detection. Such records must be available whether the INR is calculated by the coagulation instrument, laboratory information system, or manually.

It is critical to calculate and report appropriate INR values. Reporting erroneous INR values may lead to use of excessive or insufficient vitamin K antagonist medication, which may result in bleeding or thrombotic complications in patients.

Evidence of Compliance:

- ✓ Records showing that the ISI values used in the INR calculation were appropriate for new lots and types of PT reagent and for any other changes

HEM.37840 INR Geometric Mean **Phase II**

The appropriate geometric mean of the PT reference interval is used in the INR calculation.

NOTE: The appropriate geometric mean of the PT reference interval must be used in the INR calculation, given by the formula:

$$INR=(PT\ of\ patient\ /\ PT\ of\ geometric\ mean\ normal\ population)^{ISI}$$

The mean normal population value may change when the specimen collection process, instrument, reagent lot, or reagent changes.

When the distribution of values is distributed normally, the geometric mean, the arithmetic mean, the median and the mode of the population being studied are identical theoretically. These values diverge from each other, however, as the population distribution becomes more skewed. The geometric mean is a more appropriate estimate of the average value than the arithmetic mean when the population of interest is lognormally distributed because the geometric mean takes skewing into account.

Calculation of the geometric mean is indicated below; this calculation is available in many spreadsheet programs, such as Microsoft Excel.

GM = antilog [(log(X1) + log(X2) + log(X3) + . . . log(Xn))/n].

Evidence of Compliance:
- ✓ Records for geometric mean determinations and INR calculations for each instrument and PT reagent lots used

HEM.37860 Report Verification Criteria **Phase II**

Patient reports are checked for correct INR calculations, patient values, and reference intervals under the following circumstances:

1. **Change in lot or type of PT reagent**
2. **Change in instrument**
3. **Establishment of new PT reference interval**
4. **Change in INR calculation**
5. **At defined intervals, in the absence of the above changes**

NOTE: It is suggested that the calculations be checked at the following INR values: 2.0 and 3.0. Patient reports must be checked at least once per year even in the absence of changes to the test system and calculations. This requirement applies whether the INR is calculated by the coagulation analyzer or by the laboratory information system.

Evidence of Compliance:
- ✓ Records of patient report checks at defined frequency

HEM.37870 Reference Intervals **Phase II**

Reference intervals for PT and aPTT are current for the reagent or lot number, and are appropriately determined.

NOTE: Because of the variability between different types of PT and aPTT reagents, and even different lots of PT and aPTT reagents, there may be significant changes in the reference interval after a change of the type or lot of reagent. For this reason, the laboratory should establish and then verify the reference interval with each change of lot or change in reagent.

Evidence of Compliance:
- ✓ Reports showing verification of the reference interval with changes of lot or reagent **AND**
- ✓ Patient reports reflecting the use of the correct reference intervals

HEM.37880 Unfractionated Heparin Therapeutic Interval **Phase I**

The aPTT-based unfractionated heparin (UFH) therapeutic interval is established and subsequently verified using an appropriate method.

NOTE: The UFH-responsiveness of aPTT reagents may change from lot to lot and among different reagents used on different instrument platforms. For this reason, it is necessary to establish the UFH therapeutic interval for the aPTT assay with each change of coagulation instrument and/or reagent type. The therapeutic interval must be verified with each new lot of a given aPTT reagent.

The aPTT is commonly used to monitor the anticoagulant effects of UFH. The therapeutic interval for UFH therapy should be initially validated for new reagents or instruments by using ex vivo plasma samples anticoagulated with 3.2% sodium citrate obtained from patients receiving therapeutic doses of UFH. This can be accomplished by measuring the aPTT and UFH activity and then deriving the aPTT therapeutic interval by comparison to UFH activity. For subsequent reagent lot changes, the therapeutic interval can be verified by comparing the aPTT of patient samples using the new and the prior aPTT lots. It is not best practice to use plasma samples spiked with UFH in vitro to calculate the therapeutic interval, as differences in UFH binding proteins in vitro may lead to overestimation of the therapeutic interval.

Laboratories in a local care network or system using the same instrument and same lot of an aPTT reagent, can share their nomogram of UFH. However, a verification study using one laboratory as the reference laboratory to show that their results are comparable to each other must be performed.

Guidance on determining the UFH therapeutic interval using the aPTT can be found on cap.org at https://documents.cap.org/documents/heparin-sensitivity-new-aptt-reagents.pdf.

UFH assays using factor Xa inhibitory or IIa inhibitory assays are preferred alternate methods to monitor UFH therapy.

Evidence of Compliance:

- ✓ Records of establishment and verification of the aPTT UFH therapeutic interval for each lot of aPTT reagent used

D-DIMER STUDIES

HEM.37924 D-dimer Unit Results **Phase II**

The unit type (eg, FEU or D-DU) and unit of magnitude (eg, ng/mL) reported with the patient results are the same units as generated directly by the D-dimer method (following manufacturer's product insert); or if different units are reported, the laboratory verifies the correct conversion of the units on an annual basis.

NOTE: The CAP and Clinical Laboratory and Standards Institute (CLSI) recommend that units not be converted from those stated in the package insert. If units are converted, the laboratory must verify the conversion of the units in patient reports for patient values, cut-off values, and reference intervals with changes in reagents, instrument and at least once per year in the absence of a change, with records retained.

The units generated directly by the D-dimer method can be determined from the package insert. If units are not stated in the package insert, consult with the manufacturer of the D-dimer method.

The following chart demonstrates the correct conversion factor for the different reporting units:

Manufacturer Units	Final Units	Correct Conversion Factor	Equivalency Equation
FEU ng/mL	D-DU ng/mL	0.5	1 FEU ng/mL = 0.5 D-DU ng/mL
FEU ng/mL	D-DU µg/mL	0.0005	1 FEU ng/mL = 0.0005 D-DU µg/mL
FEU µg/mL	FEU ng/mL	1000	1 FEU µg/mL = 1000 FEU ng/mL
D-DU ng/mL	FEU ng/mL	2	1 D-DU ng/mL = 2 FEU ng/mL
D-DU µg/mL	FEU ng/mL	2000	1 D-DU µg/mL = 2000 FEU ng/mL
D-DU µg/mL	D-DU ng/mL	1000	1 D-DU µg/mL = 1000 D-DU ng/mL

Evidence of Compliance:

- ✓ Patient reports with unit type (FEU vs. DDU) and unit of magnitude (ng/mL vs. µg/mL) that are the same as the units directly generated by the D-dimer method and in the manufacturer's product insert **OR**
- ✓ Records of the annual verification to confirm correct conversion of the unit type (FEU vs. DDU) and unit of magnitude (ng/mL vs. µg/mL) if units are reported that are different than those directly generated by the D-dimer method

HEM.37925 D-dimer - Evaluation of VTE **Phase II**

If a quantitative D-dimer method is used in the evaluation of venous thromboembolism (VTE), the method is valid for this purpose.

NOTE: D-Dimer methods intended for evaluation of VTE may be used, along with pretest probability, if a method specific cut-off value is available. Cut-off values are not universal, so method specific data regarding the negative predictive value and the sensitivity should be available. For cut-off data acquired from the literature, the CLSI (H59-A) recommends a negative predictive value of ≥98% (lower limit of CI ≥95%) and a sensitivity of ≥97% (lower limit of CI ≥90%) for non-high pretest probability of VTE.

For D-dimer methods that are FDA-cleared/approved for exclusion of VTE, the package insert includes the cut-off value and this value should be provided in the report. It is not feasible for most laboratories to perform a sufficient clinical validation of a D-dimer cut-off for use in the evaluation of VTE (ie, either exclusion or aid in diagnosis), including separate validation of the cut-off for deep vein thrombosis and pulmonary embolism. Therefore using the cutoff supplied from the manufacturer is strongly recommended.

If a laboratory or group of laboratories determine a cut-off (not published in literature or the package insert), a summary of data including the NPV, sensitivity, and power of determination must be available. The CLSI Guideline H59-A recommends correlation with imaging studies and follow-up after three months on a minimum of 200 cases to establish the threshold for VTE exclusion.

Evidence of Compliance:

- ✓ Package insert stating an Intended Use for the exclusion of VTE or aid in the diagnosis of VTE **AND**
- ✓ A method specific cut-off for the evaluation of VTE from the package insert, literature, or an extensive clinical validation study

HEM.37930 D-dimer Reporting **Phase II**

If a D-dimer test is used for evaluation of venous thromboembolism (VTE), the laboratory reports the VTE exclusion cut-off value as stated by the manufacturer. If the D-dimer test is intended for other purposes (eg, DIC evaluation) a reference interval is required.

NOTE: This requirement only applies to quantitative D-dimer tests.

The cut-off value and upper limit of the reference interval are not always identical. The upper limit of the reference interval may be used to evaluate disseminated intravascular coagulation (DIC), while the cut-off value is used for evaluation of VTE (see COM.29950 regarding reference interval reporting). The cut-off value and/or reference interval must be reported in units identical to the patient results, including both unit type (FEU or D-DU) and unit of magnitude (eg, ng/mL).

Evidence of Compliance:

- ✓ Patient reports including both the reference interval and/or the cut-off value for VTE evaluation

HEM.37935 Sensitivity of D-dimer Test - Evaluation of VTE **Phase I**

If a D-dimer test is insufficiently sensitive to exclude venous thromboembolism, the laboratory informs clinicians that the test must not be used for this purpose.

NOTE: Manual agglutination D-dimer and FDP (fibrin degradation products) assays are not adequately sensitive for evaluation of deep vein thrombosis and/or pulmonary embolism.