



Advancing Excellence

COMMISSION ON LABORATORY ACCREDITATION

Laboratory Accreditation Program

CHEMISTRY AND TOXICOLOGY CHECKLIST

Disclaimer and Copyright Notice

The College of American Pathologists (CAP) Checklists are posted on the CAP's Web site for information only. If you are enrolled in the CAP's Laboratory Accreditation Program and are preparing for an inspection, you must use the Checklists that were mailed in your application or reapplication packet, not those posted on the Web site. The Checklists undergo regular revision and Checklists may be revised after you receive your packet.

If a Checklist has been updated since receiving your packet, you will be inspected based upon the Checklists that were mailed. If you have any questions about the use of Checklists in the inspection process, please e-mail the CAP (accred@cap.org), or call (800) 323-4040, ext. 6065.

All Checklists are ©2006. College of American Pathologists. All rights reserved.

CHEMISTRY AND TOXICOLOGY

OUTLINE

SUMMARY OF CHANGES	4
INSPECTION TECHNIQUES – KEY POINTS	6
INTRODUCTION	8
CHEMISTRY & TOXICOLOGY GENERAL ISSUES	8
PROFICIENCY TESTING	8
QUALITY MANAGEMENT AND QUALITY CONTROL	13
GENERAL ISSUES	13
PROCEDURE MANUAL	15
SPECIMEN COLLECTION AND HANDLING	18
REAGENTS	20
CALIBRATION AND STANDARDS	24
CONTROLS	32
RESULTS REPORTING	39
ANALYTIC METHODS AND PROCESSES	41
METHODS AND INSTRUMENT SYSTEMS	43
Immunoassays/Immunoanalyzers	44
Radioimmunoassays	44
Chromatography and Mass Spectrometry	45
Thin Layer Chromatography (TLC)	46
Gas Chromatography (GC)	47
High Performance Liquid Chromatography (HPLC)	50
Mass Spectrometry (MS)	53
Inductively Coupled Plasma – Mass Spectrometry (ICP/MS)	57
Atomic Absorption Spectrophotometers	61
Colorimeters and Spectrophotometers	63
Flame Photometers	64
Equipment Maintenance	64
Glassware	67
Automatic Pipettes - Fixed Volume Adjustable and/or Micropipettes	69
Thermometers	71
Temperature -Dependent Equipment	72
Centrifuges	73
Analytic Balances	74
PERSONNEL	76
PHYSICAL FACILITIES	77
LABORATORY SAFETY	81
RADIATION SAFETY	81
GENERAL CHEMISTRY	84
CHEMISTRY	84
THERAPEUTIC DRUG MONITORING	84
SWEAT TESTING FOR CYSTIC FIBROSIS	86
Specimen Collection and Handling	86
Analytic Methods for Sweat Testing	93
Reporting of Results	95
Personnel	97
PRENATAL SCREENING	97
Triple Test (Maternal serum alpha-fetoprotein (MSAFP), Unconjugated Estriol (MsuE3), (hCG)	97
Requisitions/Calculations/Reports	97
Interpretive Reporting for Maternal Screening	104
Amniotic Fluid Alpha-fetoprotein (AFAFP)	106

ELECTROPHORESIS 110
 Hemoglobin Electrophoresis 110
BLOOD GAS ANALYSIS 114
 SPECIMEN COLLECTION AND HANDLING 114
 BLOOD GAS INSTRUMENTS 115
LEGAL TESTING 117

SUMMARY OF CHANGES
CHEMISTRY AND TOXICOLOGY Checklist
4/6/2006 Edition

The following questions have been added, revised, or deleted in this edition of the checklist, or in the two editions immediately previous to this one.

If this checklist was created for a reapplication, on-site inspection or self-evaluation it has been customized based on the laboratory's activity menu. The listing below is comprehensive; therefore some of the questions included may not appear in the customized checklist. Such questions are not applicable to the testing performed by the laboratory.

Note: For revised checklist questions, a comparison of the previous and current text may be found on the CAP website. Click on Laboratory Accreditation, Checklists, and then click the column marked Changes for the particular checklist of interest.

NEW Checklist Questions

<u>Question</u>	<u>Effective Date</u>
CHM.10433	04/06/2006
CHM.10466	04/06/2006
CHM.14916	04/06/2006
CHM.13750	03/30/2005
CHM.29150	03/30/2005
CHM.30150	03/30/2005

REVISED Checklist Questions

<u>Question</u>	<u>Effective Date</u>
CHM.11000	04/06/2006
CHM.12900	10/06/2005
CHM.14100	10/06/2005
CHM.17200	10/06/2005
CHM.25500	10/06/2005
CHM.14000	03/30/2005
CHM.24100	03/30/2005
CHM.29300	03/30/2005
CHM.30900	03/30/2005

DELETED Checklist Questions

<u>Question</u>	<u>Effective Date</u>
CHM.16600	04/06/2006
CHM.17250	04/06/2006

CHM.27100	10/06/2005
CHM.33780	10/06/2005
CHM.30500	03/30/2005
CHM.27800	12/29/2004

The checklists used in connection with the inspection of laboratories by the Commission on Laboratory Accreditation (“CLA”) of the College of American Pathologists have been created by the College and are copyrighted works of the College. The College has authorized copying and use of the checklists by College inspectors in conducting laboratory inspections for the CLA and by laboratories that are preparing for such inspections. Except as permitted by section 107 of the Copyright Act, 17 U.S.C. sec. 107, any other use of the checklists constitutes infringement of the College’s copyrights in the checklists. The College will take appropriate legal action to protect these copyrights.

IMPORTANT: The contents of the Laboratory General Checklist are applicable to the Chemistry and Toxicology section of the laboratory.

INSPECTION TECHNIQUES – KEY POINTS

I. READ – OBSERVE – ASK – the three methods of eliciting information during the inspection process. These three methods may be used throughout the day in no particular order. Plan the inspection in a way that allows adequate time for all three components.

READ = Review of Records and Documents

Document review verifies that procedures and manuals are complete, current, available to staff, accurate and reviewed, and describe good laboratory practice. Make notes of any questions you may have, or processes you would like to observe as you read the documentation.

OBSERVE – ASK = Direct Observation and Asking Questions

Observing and asking questions accomplish the following:

1. Verifies that the actual practice matches the written policy or procedure
2. Ensures that the laboratory processes are appropriate for the testing performed
3. Ensures that outcomes for any problem areas, such as PT failures and issues/problems identified through the quality management process, have been adequately investigated and resolved
4. Ensures that previously cited deficiencies have been corrected

Use the following techniques:

- **Observe laboratory practices** – look at what the laboratory is actually doing. Compare the written policy/procedure to what you actually observe in the laboratory to ensure the written policy/procedure accurately reflects laboratory practice. Note if practice deviates from the documented policies/procedures.
- **Ask open ended, probing questions** – these are starting points that will allow you to obtain large amounts of information, and help you clarify your understanding of the documentation you’ve seen

and observations you've made. This eliminates the need to ask every single checklist question, as the dialogue between you and the laboratory may address multiple checklist questions.

- Ask open-ended questions that start with phrases such as “show me how...” or “tell me about ...” or “what would you do if...”. By asking questions that are open-ended, or by posing a hypothetical problem, you will avoid “cookbook” answers. For example, ask “Could you show me the specimen transport policy and show me how you ensure optimum specimen quality?” This will help you to determine how well the technical staff is trained, whether or not they are adhering to the lab’s procedures and policies, and give you a feel for the general level of performance of the laboratory.
- Ask follow-up questions for clarification. Generally, it is best not to ask the checklist questions verbatim. For example, instead of asking the checklist question “Is there documentation of corrective action when control results exceed defined tolerance limits?” ask, “What would you do if the SD or CV doubles one month?” A follow-up probing question could be, “What would you do if you were unable to find a cause for the change in SD or CV?”

II. Evaluate Selected Specimens and Tests in Detail

For the Laboratory General Checklist: Follow a specimen through the laboratory. By following a specimen from collection to test result, you can cover multiple checklist questions in the Laboratory General checklist: questions on the specimen collection manual; phlebotomy; verbal orders; identification of patients and specimens; accessioning; and result reporting, including appropriate reference ranges, retention of test records, maintaining confidentiality of patient data, and proper handling of critical values and revisions to reports.

For the individual laboratory sections: Consult the laboratory’s activity menu and focus on tests that potentially have the greatest impact on patient care. Examples of such tests include HIV antibodies, hepatitis B surface antigen, urine drugs of abuse, quantitative beta-hCG, cultures of blood or CSF, acid-fast cultures, prothrombin time and INR reporting, and compatibility testing and unexpected antibody detection. Other potentially high-impact tests may be identified by looking at very high or low volume tests in the particular laboratory, or problems identified by reviewing the Variant Proficiency Testing Performance Report.

To evaluate preanalytic and postanalytic issues: Choose a representative specimen and “follow” the specimen through the laboratory or section of the laboratory, reviewing appropriate records in the preanalytic and postanalytic categories.

To evaluate analytic processes: Choose 2 or 3 analytes and perform a comprehensive review of records, including procedure manuals, quality control and proficiency testing records, instrument maintenance records and method performance validations for the last 2 years, selecting timeframes at the beginning, mid-point, and end of this timeframe. Compare instrument print-outs to patient reports and proficiency testing results to ensure accurate data entry. If problems are identified, choose additional tests or months to review.

III. Verify that proficiency testing problem have been resolved: From the inspector’s packet, review the Variant PT Performance Report that identifies, by analyte, all of the PT scores below 100%. Correlate any PT problems to QC or maintenance records from the same time period. Be thorough when reviewing these representative records, selecting data from the beginning, middle and end of the period since the last on-site inspection.

IV. Review correction of previous deficiencies: Review the list of deficiencies from the previous on-site inspection provided in the inspector’s packet. Ensure that they have been appropriately addressed.

INTRODUCTION

The College of American Pathologists (CAP) recognizes that each laboratory may have different physical and functional groupings of routine automated chemistry assays, specialized chemistry procedures, and toxicology procedures. This may create mismatches between the contents of this checklist and the way a particular laboratory is organized. This Checklist is now revised to incorporate the previous Toxicology and Special Chemistry Checklists. The specific sections requiring completion depends on the specific testing repertoire of the laboratory. The Laboratory General Checklist also must be completed.

This Checklist is intended for comprehensive clinical chemistry testing, including blood gas analysis and toxicology.

#####

CHEMISTRY & TOXICOLOGY GENERAL ISSUES

#####

PROFICIENCY TESTING

CHM.10000 Phase II N/A YES NO

Is the laboratory enrolled in the appropriate required CAP Surveys or CAP-approved alternative proficiency testing (PT) program for the patient/client testing performed?

NOTE: The list of analytes for which CAP requires proficiency testing is available on the CAP website

[http://www.cap.org/apps/docs/laboratory_accreditation/checklists/checklist_reference_links.doc] or by phoning 800-323-4040 (or 847-832-7000), option 1. The laboratory's participation in proficiency testing must include all analytes on this list for which it performs patient testing. Participation in proficiency testing may be through CAP Surveys or a CAP-approved proficiency testing provider. Laboratories will not be penalized if they are unable to enroll in an oversubscribed program. If unable to enroll, however, the laboratory must implement an alternative assessment procedure for the affected analytes. For regulated analytes, if the CAP and CAP-approved alternative PT programs are oversubscribed, CMS requires the laboratory to attempt to enroll in another CMS-approved PT program.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7146 [42CFR493.801]; 2) Tholen DW. Reference values and participant means as targets in proficiency testing. *Arch Pathol Lab Med*. 1993;117:885-889; 3) Borsotti M. External quality assessment scheme in Tuscany, Italy. *Ann Ist Super Sanita*. 1995;31:175-186; 4) Westgard JO, *et al*. Laboratory precision performance. State of the art versus operating specifications that assure the analytical quality required by clinical laboratory improvement amendments proficiency testing. *Arch Pathol Lab Med*. 1996;120:621-625; 5) NCCLS. Continuous quality improvement: essential management approaches and their use in proficiency testing; proposed guideline GP22-P. Wayne, PA: NCCLS, 1997; 6) Ross JW, *et al*. The accuracy of laboratory measurements in clinical chemistry. A study of 11 routine chemistry analytes in the College of American Pathologists chemistry survey with fresh frozen serum, definitive methods, and reference materials. *Arch Pathol Lab Med*. 1998;122:587-608; 7) College of American Pathologists, Commission on Laboratory Accreditation. Standards for laboratory accreditation; standard III. Northfield, IL: CAP, 1998; 8) Dale JC, Hamrick HJ. Neonatal bilirubin testing practices. Reports from 312 laboratories enrolled in the College of American Pathologists Excel proficiency testing program. *Arch Pathol Lab Med*. 2000;124:1425-1428; 9) Plebani M, *et al*. External quality assessment for serum proteins: state of the art. *Clin Chem*. 2001;47(suppl):A35; 10) Panteghini M, *et al*. External quality assessment scheme for biochemical markers of cardiac damage. *Clin Chem*. 2001;47(suppl):A195; 11) Wilson JF, *et al*. Primary standardization of assays for anticonvulsant drugs: comparison of accuracy and precision. *Clin Chem*. 2002;48:1963-1969; 12) Taylor A, *et al*. Comparison of procedures for evaluating laboratory performance in external quality assessment schemes for lead in blood and aluminum in serum demonstrates the need for common quality specifications. *Clin Chem*. 2002;48:2000-2007.

CHM.10100

Phase II

N/A YES NO

For tests for which CAP does not require PT, does the laboratory at least semiannually 1) participate in external PT, or 2) exercise an alternative performance assessment system for determining the reliability of analytic testing?

NOTE: Appropriate alternative performance assessment procedures may include: split sample analysis with reference or other laboratories, split samples with an established in-house method, assayed material, regional pools, clinical validation by chart review, or other suitable and documented means. It is the responsibility of the laboratory director to define such alternative performance assessment procedures, as applicable, in accordance with good clinical and scientific laboratory practice. Participation in ungraded/educational proficiency testing programs also satisfies this checklist question.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7184 [42CFR493.1236(c)(1)]; 2) Shahangian S, *et al*. A system to monitor a portion of the total testing process in medical clinics and laboratories. Feasibility of a split-specimen design. *Arch Pathol Lab Med*. 1998;122:503-511; 3) Shahangian S, Cohn RD. Variability of laboratory test results. *Am J Clin Pathol*. 2000;113:521-527; 4) NCCLS. Assessment of laboratory tests when proficiency testing is not available; approved guideline. NCCLS document GP29-A. [ISBN 1-56238-479-1]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2002; 5) Marks V. False-positive immunoassay results: a multicenter survey of erroneous immunoassay results from assays of 74 analytes in 10 donors from 66 laboratories in seven countries. *Clin Chem*. 2002;48:2008-2016.

CHM.10200

Phase II

N/A YES NO

Does the laboratory integrate all proficiency testing samples within the routine workload, and are those samples analyzed by personnel who routinely test patient/client samples, using the same primary method systems as for patient/client samples?

NOTE: Replicate analysis of any proficiency sample is acceptable only if patient/client specimens are routinely analyzed in the same manner. If the laboratory uses multiple methods for an analyte, proficiency samples should be analyzed by the primary method. There must not be any interlaboratory communication on proficiency testing data before results reporting. The educational purposes of proficiency testing are best served by a rotation that allows all technologists to be involved in the proficiency testing program. Records of these studies must be kept and can be an important part of the competency and continuing education documentation in the personnel files of the individuals. When external proficiency testing materials are not available, the semi-annual alternative performance assessment process should also be integrated within the routine workload.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7146 [42CFR493.801(b)]; 2) Shahangian S, *et al*. Toward optimal PT use. *Med Lab Observ*. 2000;32(4):32-43; 3) Parsons PJ. Evaluation of blood lead proficiency testing: comparison of open and blind paradigms. *Clin Chem*. 2001;47:322-330.

CHM.10300**Phase II****N/A YES NO**

Is there evidence of evaluation and, if indicated, prompt corrective action in response to "unacceptable" results on the proficiency testing report and results of the alternative performance assessment system?

NOTE: The evaluation must document the specific reason(s) for the "unacceptable" result(s) and actions taken to reduce the likelihood of recurrence. This must be done within one month after the laboratory receives its proficiency testing evaluation. Also, the laboratory must review its results, and institute corrective action as appropriate, for challenges that were intended to be graded, but for which no grade was received (for example, because the laboratory did not submit its results, used the incorrect method code, or because of lack of consensus).

COMMENTARY:

N/A

REFERENCES: 1) Ehrmeyer SS, *et al*. Use of alternative rules (other than the 1-2s) for evaluating interlaboratory performance data. *Clin Chem*. 1988;34:250-256; 2) Klee GG, Forsman RW. A user's classification of problems identified by proficiency testing surveys. *Arch Pathol Lab Med*. 1988;112:371-373; 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7173 [42CFR493.1407(e)(4)(iv)]; 4) Steindel SJ, *et al*. Reasons for proficiency testing failures in clinical chemistry and blood gas analysis. A College of American Pathologists Q-Probes study in 655 laboratories. *Arch Pathol Lab Med*. 1996;120:1094-1101; 5) NCCLS. Using proficiency testing (PT) to improve the clinical laboratory; approved guideline. NCCLS Document GP27-A. [ISBN 1-56238-381-7]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA: NCCLS, 1998 19087-1898, USA, 1999; 6) Shahangian S, *et al*. Toward optimal PT use. *Med Lab Observ*. 2000;32(4):32-43.

CHM.10400**Phase II****N/A YES NO**

Is there documented evidence of ongoing evaluation by the laboratory director or designee of the proficiency testing and alternative performance assessment results?

COMMENTARY:

N/A

QUALITY MANAGEMENT AND QUALITY CONTROL

GENERAL ISSUES

CHM.10500 Phase II

N/A YES NO

Does the chemistry laboratory have a written quality management/quality control (QM/QC) program?

NOTE: The QM/QC program in the chemistry laboratory must be clearly defined and documented. The program must ensure quality throughout the preanalytic, analytic, and post-analytic (reporting) phases of testing, including patient identification and preparation; specimen collection, identification, preservation, transportation, and processing; and accurate, timely result reporting. The program must be capable of detecting problems in the laboratory’s systems, and identifying opportunities for system improvement. The laboratory must be able to develop plans of corrective/preventive action based on data from its QM system.

All QM questions in the Laboratory General Checklist pertain to the chemistry laboratory.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7176 [42CFR493.1445(e)(5).

CHM.10600 Phase II

N/A YES NO

Is there a documented procedure describing methods for patient/client identification, patient/client preparation, specimen collection and labeling, specimen preservation, and conditions for transportation, and storage before testing, consistent with good laboratory practice?

COMMENTARY:

N/A

CHM.10700 Phase II**N/A YES NO**

Is there evidence of ongoing evaluation of records of controls, instrument maintenance and function, temperature, etc., for all procedures as required?

COMMENTARY:

N/A

CHM.10800 Phase II**N/A YES NO**

Is there a documented system in operation to detect and correct significant clerical and analytical errors, and unusual laboratory results, in a timely manner?

NOTE: The laboratory must have a documented system in operation to detect and correct significant clerical and analytical errors, and unusual laboratory results. One common method is review of results by a qualified person (technologist, supervisor, pathologist) before release from the laboratory, but there is no requirement for supervisory review of all reported data. The selective use of delta checks also may be useful in detecting clerical errors in consecutive samples from the same patient/client. In computerized laboratories, there should be automatic "traps" for improbable results. The system for detecting clerical errors, significant analytical errors, and unusual laboratory results must provide for timely correction of errors, i.e., before results become available for clinical decision making. For suspected errors detected by the end user after reporting, corrections must be promptly made if such errors are confirmed by the laboratory.

Each procedure must include a listing of common situations that may cause analytically inaccurate results, together with a defined protocol for dealing with such analytic errors or interferences. This may require alternate testing methods; in some situations, it may not be possible to report results for some or all of the tests requested.

The intent of this requirement is NOT to require verification of all results outside the reference (normal) range.

COMMENTARY:

N/A

REFERENCE: Dufour D, et al. The clinical significance of delta checks. *Am J Clin Pathol.* 1998;110:531.

CHM.10900

Phase II

N/A YES NO

Are the results of tests performed in the absence of on-site supervisors reviewed by the laboratory director or general supervisor within 24 hours?

NOTE: The CAP does NOT require supervisory review of all test results. This question addresses only that situation defined under CLIA-88 for "high complexity testing" performed by trained high school graduates qualified under 42CFR493.1489(b)(5) when a qualified general supervisor is not present.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7182 [42CFR493.1463(a)(3) and 42CFR493.1463(c)]: 7183 [42CFR493.1489(b)(1) and 42CFR493.1489(b)(5)].

PROCEDURE MANUAL

The procedure manual should be used by personnel at the workbench and should include: test principle, clinical significance, specimen type, required reagents, test calibration, quality control, procedural steps, calculations, reference intervals, and interpretation of results. The manual should address relevant pre-analytic and post-analytic considerations, as well as the analytic activities of the laboratory. The specific style and format of procedure manuals are at the discretion of the laboratory director.

The inspection team should review the procedure manual in detail to understand the laboratory's standard operating procedures, ensure that all significant information and instructions are included, and that actual practice matches the contents of the procedure manuals.

****REVISED**** **04/06/2006**

CHM.11000

Phase II

N/A YES NO

Is a complete procedure manual available at the workbench or in the work area?

NOTE 1: The use of inserts provided by manufacturers is not acceptable in place of a procedure manual. However, such inserts may be used as part of a procedure description, if

the insert accurately and precisely describes the procedure as performed in the laboratory. Any variation from this printed or electronic procedure must be detailed in the procedure manual. In all cases, appropriate reviews must occur.

NOTE 2: A manufacturer's procedure manual for an instrument/reagent system may be acceptable as a component of the overall departmental procedures. Any modification to or deviation from the procedure manual must be clearly documented.

NOTE 3: Card files or similar systems that summarize key information are acceptable for use as quick reference at the workbench provided that:

- a. A complete manual is available for reference*
- b. The card file or similar system corresponds to the complete manual and is subject to document control*

NOTE 4: Electronic (computerized) manuals are fully acceptable. There is no requirement for paper copies to be available for the routine operation of the laboratory, so long as the electronic versions are readily available to all personnel. However, procedures must be available to laboratory personnel when the electronic versions are inaccessible (e.g., during laboratory information system or network downtime); thus, the laboratory must maintain either paper copies or electronic copies on CD or other media that can be accessed via designated computers. Current paper copies of electronically stored procedures should be available at the time of the CAP inspection, or rapidly generated at the request of the inspector.

Electronic versions of procedures must be subjected to proper document control (i.e., only authorized persons may make changes, changes are dated/signed (manual or electronic), and there is documentation of annual review). Documentation of review of electronic procedures may be accomplished by including statements such as "reviewed by [name of reviewer] on [date of review]" in the electronic record. Alternatively, paper review sheets may be used to document review of electronic procedures. Documentation of review by a secure electronic signature is NOT required.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7164 [42CFR493.1251(a) (b) (1-14)(c)(d)(e)]; 2) van Leeuwen AM. 6 Steps to building an efficiency tool. *Advance/Laboratory*. 1999;8(6):88-91; 3) Borkowski A, *et al*. Intranet-based quality improvement documentation at the Veterans Affairs Maryland health care system. *Mod. Pathol*. 2001;14:1-5; 4) NCCLS. Clinical laboratory technical procedure manuals - fourth edition; approved guideline GP2-A4. Wayne, PA: NCCLS, 2002.

CHM.11800	Phase II	N/A	YES	NO
------------------	-----------------	------------	------------	-----------

Are procedures adequate to verify the identity and integrity of samples, including capillary specimens, aliquots and dilutions?

COMMENTARY:

N/A

CHM.11900	Phase II	N/A	YES	NO
------------------	-----------------	------------	------------	-----------

Are there documented criteria for the rejection of unacceptable specimens and instructions for the special handling of sub-optimal specimens?

NOTE: This question does not imply that all "unsuitable" specimens are discarded or not analyzed. If, for example, a serum potassium or lactate dehydrogenase is ordered and the blood sample is hemolyzed, there must be a mechanism to notify clinical personnel responsible for patient care. If the treating physician desires the result, then the laboratory must note the condition of the sample on the report. Some or all tests may not be analytically valid on such a specimen. The laboratory may wish to record that a dialogue was held with the physician, when such occurs.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7183 [42CFR493.1249(a) and (b)]; 2) Jones BA, et al. Chemistry specimen acceptability. A College of American Pathologists Q-Probes study of 453 laboratories. *Arch Pathol Lab Med*. 1997;121:19-26; 3) Hill DM, et al. Effects of temperature on stability of blood homocysteine in collection tubes containing 3-deazaadenosine. *Clin Chem*. 2002;48:2017-2022; 4) Kiliç AS, et al. Falsely increased free triiodothyronine in sera stored in serum separator tubes. *Clin Chem*. 2002;48:2296-2297.

CHM.12000	Phase II	N/A	YES	NO
------------------	-----------------	------------	------------	-----------

Is the disposition of all unacceptable specimens documented in the patient/client report and/or quality management records?

NOTE: This information is essential to proper patient/client test management and to the laboratory quality management program.

COMMENTARY:

N/A

CHM.12133 Phase II

N/A YES NO

Does the documented aliquoting procedure prevent cross-contamination of specimens and aliquots?

NOTE: Certain limited volume specimens may warrant the use of previously aliquotted specimens. In such cases, the laboratory must have a clearly defined, documented policy specifying such circumstances and a procedure describing how it is performed.

COMMENTARY:

N/A

CHM.12266 Phase II

N/A YES NO

Is the aliquoting procedure properly followed by the staff?

NOTE: The inspector should observe the aliquoting process to determine whether the documented procedure is satisfactory and being followed to prevent cross-contamination and specimen mix-ups.

COMMENTARY:

N/A

REAGENTS

Verification of reagent performance is required. The intent of the questions is that reagents are used according to manufacturer's instructions and new reagents are checked by an appropriate method before being placed in service. Results of reagent checks must be documented. Where individually packaged reagents/kits are used, criteria should be established for monitoring reagent quality and stability, based on volume of usage and storage requirements.

CHM.12400 Phase II

N/A YES NO

Are reagents and solutions properly labeled, as applicable and appropriate, with the following elements?

- 1. Content and quantity, concentration or titer**

2. **Storage requirements**
3. **Date prepared or reconstituted by laboratory**
4. **Expiration date**

NOTE: The above elements may be recorded in a log (paper or electronic), rather than on the containers themselves, providing that all containers are identified so as to be traceable to the appropriate data in the log. While useful for inventory management, labeling with "date received" is not routinely required. There is no requirement to routinely label individual containers with "date opened"; however, a new expiration date must be recorded if opening the container changes the expiration date, storage requirement, etc. The inspector will describe specific issues of non-compliance in the Inspector's Summation Report.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7164 [42CFR493.1252(c)]; 2) Gonzales Y, Kampa IS. The effect of various storage environments on reagent strips. *Lab Med*. 1997;28:135-137; 3) NCCLS. Clinical laboratory technical procedure manuals - fourth edition; approved guideline GP2-A4. Wayne, PA: NCCLS, 2002.

CHM.12500 Phase II N/A YES NO

Are all reagents stored as recommended by the manufacturer?

NOTE: Reagents must be stored as recommended by the manufacturer to prevent environmentally-induced alterations that could affect test performance. If ambient storage temperature is indicated, there must be documentation that the defined ambient temperature is maintained and corrective action taken when tolerance limits are exceeded.

COMMENTARY:

N/A

REFERENCE: Gonzales Y, Kampa IS. The effect of various storage environments on reagent strips. *Lab Med*. 1997;28:135-137.

CHM.12600 Phase II N/A YES NO

Are all reagents used within their indicated expiration date?

NOTE: The laboratory must assign an expiration date to any reagents that do not have a manufacturer-provided expiration date. The assigned expiration date should be based on known stability, frequency of use, storage conditions, and risk of deterioration.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7164 [42CFR493.1252(d)].

CHM.12700 **Phase I** **N/A YES NO**

Are common interferences evaluated for all analytes measured with each reagent system, or is credible information available?

NOTE: Common interferences should be documented for each analyte measured with each reagent system. Documentation from information in the literature is acceptable as long as the information is specific for the reagent system in use in the laboratory.

COMMENTARY:

N/A

REFERENCES: 1) Letellier G, Dejarlais F. Analytic interference of drugs in clinical chemistry. 1: Study of twenty drugs on seven different instruments. *Clin Biochem*. 1985;18:345-351; 2) NCCLS. Interference testing in clinical chemistry; approved guideline EP7-A. Wayne, PA: NCCLS, 2002; 3) Kroll MH, Elin RJ. Interference with clinical laboratory analyses. *Clin Chem*. 1994;40:1996-2005; 4) Kazmierczak SC, Catrou PG. Analytical interference. More than just a laboratory problem. *Am J Clin Pathol*. 2000;113:9-11; 5) Tang Z, et al. Effects of drugs on glucose measurements with handheld glucose meters and a portable glucose analyzer. *Am J Clin Pathol*. 2000;113:75-80; 6) Tang Z, et al. Effects of pH on glucose measurements with handheld glucose meters and a portable glucose analyzer for point-of-care testing. *Arch Pathol Lab Med*. 2000;124:577-582; 7) Young DS. Effects of drugs on clinical laboratory tests, 5th ed. Washington, DC: American Association for Clinical Chemistry, 2000.

CHM.12800 **Phase II** **N/A YES NO**

If there are multiple components of a reagent kit, does the laboratory use components of reagent kits only within the kit lot unless otherwise specified by the manufacturer?

COMMENTARY:

N/A

****REVISED**** **10/06/2005****CHM.12900** **Phase II** **N/A YES NO****Are new reagent lots and/or shipments validated before or concurrent with use for patient testing?**

NOTE: New reagent lots and/or shipments must be tested in parallel with old lots before or concurrently with being placed in service to ensure that the calibration of the new lot of reagent has maintained consistent results for patient specimens. Good clinical laboratory science includes patient-based comparisons when possible, since it is patient specimens that are tested. For quantitative tests, reagent validation is most reliably performed by assaying the same patient specimens with both the old and new lots to ensure consistent results. For qualitative tests, minimum cross-checking includes retesting at least one known positive and one known negative patient sample from the old reagent lot against the new reagent lot, ensuring that the same results are obtained with the new lot. A weakly positive sample should also be used in systems where patient results are reported in that fashion.

Some method manufacturers provide reference materials or QC products specifically intended to validate successful calibration of their methods; these should be used when available. Such materials have method-specific, and, where appropriate, reagent-lot-specific, target values. Thus, these materials should be used only with the intended methods.

Proficiency testing materials with peer group established mean values are acceptable for validation of new reagent lots.

Third party general purpose reference materials may be suitable for validation of calibration following reagent lot changes if the material is documented in the package insert or by the method manufacturer to be commutable with patient specimens for the method. A commutable reference material is one that gives the same numeric result as would a patient specimen containing the same quantity of analyte in the analytic method under discussion; e.g., matrix effects are absent. Commutability between a reference material and patient specimens can be demonstrated using the protocol in NCCLS EP14-A2.

QC material may be an acceptable alternative for validating calibration following reagent lot changes. However, the laboratory should be aware that QC material may be affected by matrix interference between different reagent lots. Thus, even if QC results show no change following a reagent lot change, a calibration inconsistency for patient specimens could exist nonetheless, masked by matrix interference affecting the QC material (a "false negative" validation). The use of patient samples to confirm the absence of matrix interference may be helpful.

It is acceptable to use QC material alone to check a new shipment of a reagent lot currently in use, as there should be no change in potential matrix interactions between QC material and different shipments of the same lot number of reagent.

COMMENTARY:

N/A

REFERENCE: Clinical and Laboratory Standards Institute. *Evaluation of Matrix Effects; Approved Guideline—Second Edition*. CLSI document EP14-A2 (ISBN 1-56238-561-5). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 190871898, USA, 2005.

CALIBRATION AND STANDARDS

This introduction discusses the processes of calibration, calibration verification, and analytical measurement range validation (AMR).

CALIBRATION is the set of operations that establish, under specified conditions, the relationship between reagent system/instrument response and the corresponding concentration/activity values of an analyte. Calibration procedures are typically specified by a method manufacturer, but may also be established by the laboratory.

The term “calibration” has the same meaning in this checklist as in the U.S. CLIA-88 regulations.

However, the term “calibration verification,” as used in this checklist, carries a more restrictive meaning than in CLIA-88. As defined in the January, 2003 revision of CLIA-88, “calibration verification” refers to 2 distinct processes: 1) verification of correct method calibration and 2) validation of the reportable range. This checklist restricts the use of the term “calibration verification” to the first process. The checklist uses a different term, “analytical measurement range (AMR) validation,” to refer to the second process.

All of these processes—calibration, calibration verification, and AMR validation—are required to ensure the continued accuracy of a test method. These concepts are further elaborated below.

In this checklist, CALIBRATION VERIFICATION denotes the process of confirming that the current calibration settings remain valid for a method. If calibration verification confirms that the current calibration settings are valid, it is not necessary to perform a complete calibration or recalibration of the method. Calibration verification can be accomplished in several ways. If the method manufacturer provides a calibration validation or verification process, it should be followed. Other techniques include (1) assay of the current method calibration materials as unknown specimens, and determination that the correct target values are recovered, and (2) assay of matrix-appropriate materials with target values that are specific for the method.

Each laboratory must define limits for accepting or rejecting tests of calibration verification.

Materials for calibration verification must have a matrix appropriate for the clinical specimens assayed by that method, and target values appropriate for the measurement system. Materials may include, but are not limited to:

- 1. Calibrators used to calibrate the analytical measurement system*
- 2. Materials provided by the analytical measurement system vendor 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. Proficiency testing material or proficiency testing validated material with matrix characteristics and target values appropriate for the method*

In general, routine control materials are not suitable for calibration verification, except in situations where the material is specifically designated by the method manufacturer as suitable for verification of the method's calibration process.

The ANALYTICAL MEASUREMENT RANGE (AMR) is the range of analyte values that a method can directly measure on the specimen without any dilution, concentration, or other pretreatment not part of the usual assay process. AMR VALIDATION is the process of confirming that the assay system will correctly recover the concentration or activity of the analyte over the AMR. The materials used for validation must be known to have matrix characteristics appropriate for the method. The matrix of the sample (i.e., 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. The test specimens must have analyte values which, at a minimum, are near the low, midpoint, and high values of the AMR. Specimen target values can be established by comparison with peer group values for reference materials, by assignment of reference or comparative method values, and by dilution or admixture ratios of one or more specimens with known values. Each laboratory must define limits for accepting or rejecting validation tests of the AMR.

Materials for AMR validation should have a matrix appropriate for the clinical specimens assayed by that method, and target values appropriate for the measurement system. Materials may include, but are not limited to:

- 1. Linearity material of appropriate matrix, e.g., CAP Survey-based or other suitable linearity verification material*
- 2. Proficiency testing survey material or proficiency testing survey-validated material*
- 3. Previously tested patient/client specimens, unaltered*
- 4. Previously tested patient/client specimens, altered by admixture with other specimens, dilution, spiking in known amounts of an analyte, or other technique*
- 5. Primary or secondary standards or reference materials with matrix characteristics and target values appropriate for the method*
- 6. Calibrators used to calibrate the analytic measurement system*
- 7. Control materials, if they adequately span the AMR.*

RECALIBRATION / CALIBRATION VERIFICATION and AMR VALIDATION INTERVALS:
Recalibration or calibration verification, and AMR validation, must be performed at least once every 6 months, as specified under CLIA-88 regulations at 42CFR493.1255(b)(3). Successful calibration verification certifies that the calibration is still valid; unsuccessful calibration verification requires remedial action, which usually includes recalibration and AMR revalidation. The performance of recalibration or a calibration verification procedure resets the calendar to a new maximum 6-month interval before the next required reassessment. Methods that are recalibrated more frequently than every 6 months do not require a separate calibration verification procedure.

In addition to the every 6 month requirement, laboratories must perform recalibration or calibration verification and AMR validation at changes in major system components, and at changes of lots of chemically or physically active reagents unless the laboratory can demonstrate that changing reagent lot numbers does not affect the range used to report patient/client test results. The laboratory director should determine what constitutes a major system component change or a change in reagents that would require calibration verification and revalidation of the AMR. Manufacturers' instructions should be followed.

The laboratory should establish other criteria, as appropriate, for recalibration/calibration verification. These include but are not limited to failure of quality control to meet established criteria, and major maintenance or service to the instrument.

CHM.13000**Phase II****N/A YES NO**

Are calibration procedures for each method adequate, and are the calibration results documented?

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare & Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 1992(Feb 28):7165 [42CFR493.1217]; 2) Department of Health and Human Services, Centers for Medicare & Medicaid Services. Medicare, Medicaid and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications; final rule. *Fed Register*. 2003(Jan 24):3707 [42CFR493.1255]; 3) Kroll MH, Emancipator K. A theoretical evaluation of linearity. *Clin Chem*. 1993;39:405-413; 4) Clinical and Laboratory Standards Institute. *Evaluation of Matrix Effects; Approved Guideline—Second Edition*. CLSI document EP14-A2 (ISBN 1-56238-561-5). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 190871898, USA, 2005; 5) Miller WG. "Quality control." *Professional Practice in Clinical Chemistry: A Companion Text*, ed DR Dufour. Washington, DC: AACC Press, 1999:12-1 to 12-22; 6) Kroll MH, *et al*. Evaluation of the extent of nonlinearity in reportable range studies. *Arch Pathol Lab Med*. 2000;124:1331-1338.

CHM.13100 Phase II N/A YES NO**Are high quality materials with method- and matrix-appropriate target values used for calibration and calibration verification whenever possible?**

NOTE: Calibration materials establish the relationship between method/instrument response and the corresponding concentration/activities of an analyte. They 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.

COMMENTARY:

N/A

REFERENCE: Clinical and Laboratory Standards Institute. *Evaluation of Matrix Effects; Approved Guideline—Second Edition*. CLSI document EP14-A2 (ISBN 1-56238-561-5). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 190871898, USA, 2005.

CHM.13125 Phase II N/A YES NO**Are all calibration materials used for non-FDA cleared assays documented as to quality?**

NOTE: Standards used to prepare calibrators for non-FDA-cleared assays require certificates of purity from the vendor, or a check on purity as part of the initial assay validation process. The laboratory should document the accuracy of a new lot of calibrators by checking the new lot against the current lot .

COMMENTARY:

N/A

CHM.13175 Phase II N/A YES NO**If the laboratory handles pure controlled substances, is there a current Drug Enforcement Administration (DEA) license?**

NOTE: A U.S. laboratory handling pure controlled substance(s) must possess a current Drug Enforcement Administration (DEA) license. It is not necessary to have a DEA license if controlled substances are analyzed, only if they are possessed in pure form. Many manufacturers prepare commercial solutions of controlled substances. It may not be necessary to have a DEA license to purchase these. This checklist question is applicable only to U.S. laboratories.

COMMENTARY:

N/A

CHM.13200 Phase II

N/A YES NO

Are all calibration materials properly labeled as to content and calibration values?

NOTE: Complete values need not necessarily be recorded directly on each vial of calibrator material, so long as there is a clear indication where specific values may be found for each analyte tested and each analyzer used by the laboratory.

COMMENTARY:

N/A

CHM.13300 Phase II

N/A YES NO

Do calibration materials include dates placed in service and expiration dates?

NOTE: The dates may be recorded in a log (paper or electronic), rather than on the containers themselves, providing that all containers are identified so as to be traceable to the appropriate data in the log.

COMMENTARY:

N/A

CHM.13400 Phase II

N/A YES NO

Are criteria established for frequency of recalibration or calibration verification, and the acceptability of results?

NOTE: Criteria typically include:

1. *At changes of reagent lots for chemically or physically active or critical components, unless the laboratory can demonstrate that the use of different lots does not affect the accuracy of patient/client test results and the range used to report patient/client test data*
2. *QC fails to meet established criteria*
3. *After major maintenance or service*
4. *When recommended by the manufacturer*
5. *At least every 6 months*

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3707[42CFR493.1255(b)(3)]; 2) Miller WG. "Quality control." *Professional Practice in Clinical Chemistry: A Companion Text*, ed DR Dufour. Washington, DC: AACC Press, 1999:12-1 to 12-22.

CHM.13500**Phase II****N/A YES NO**

Is the method system recalibrated when calibration verification fails to meet the established criteria of the laboratory?

COMMENTARY:

N/A

CHM.13600**Phase II****N/A YES NO**

Is validation of the analytical measurement range (AMR) performed with matrix-appropriate materials which include the low, mid and high range of the AMR, and is the process documented?

NOTE: Calibration, calibration verification, and validation of the analytical measurement range (AMR) are required to substantiate the continued accuracy of a test method. The CLIA-88 regulations use the term "calibration verification" to refer to both verification of correct method calibration and validation of the analytical measurement range. This Checklist uses separate terms to identify two distinct processes that are both required for good laboratory practice.

The AMR is 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. Validation of the AMR is the process of confirming that the assay system will correctly recover the concentration or activity of the analyte over the AMR. The materials used for validation must be known to have matrix characteristics appropriate for the method. The test specimens must have analyte values that as a minimum are near the low, midpoint, and high values of the AMR. Guidelines for analyte levels near the low and high range of the AMR should be determined by the laboratory director. Factors to consider 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 (e.g., T-uptake, free thyroxine, free phenytoin, prolactin, FSH, troponin, pO₂). In such cases, reasonable procedures should be adopted based on available specimen materials. The method manufacturer's instructions for validating the AMR should be followed, when available. Specimen target values can be established by comparison

with peer group values for reference materials, by assignment of reference or comparison method values, and by dilution ratios of one or more specimens with known values. Each laboratory must define limits for accepting or rejecting validation tests of the AMR. The AMR must be revalidated at least every 6 months, and following changes in major system components or lots of analytically critical reagents (unless the laboratory can demonstrate that changing reagent lot numbers does not affect the range used to report patient test results, and control values are not adversely affected).

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3707 [42CFR493.1255].

CHM.13700**Phase II****N/A YES NO**

Are criteria established for validating the analytical measurement range, and is compliance documented?

NOTE: If the materials used for calibration or for calibration verification include low, midpoint, and high values that are near the stated AMR, and if calibration verification data are within the laboratory's acceptance criteria, the AMR has been validated; no additional procedures are required. If the calibration and/or calibration verification materials do not span the full AMR, or the laboratory extends the AMR beyond the manufacturer's stated range, the AMR must be validated by assaying materials reasonably near the lowest and highest values of the AMR.

Some instruments have integral automatic dilution systems when a result exceeds the AMR. Validation of the AMR refers to the inherent measurement range of the method, not to the range extended by an automatic dilution process. A separate validation of the automatic dilution process should be performed.

COMMENTARY:

N/A

****NEW******03/30/2005****CHM.13750****Phase I****N/A YES NO**

For qualitative tests that use a cut-off value to distinguish positive from negative, is the cut-off value established initially, and verified every 6 months thereafter?

NOTE: This checklist question applies only to tests that report qualitative results based on a quantitative measurement using a threshold (cut-off value) to discriminate between a positive and negative clinical interpretation (for example, tests for viral hepatitis markers or urine drugs of abuse). The cut-off value that distinguishes a positive from a negative result should be established when the test is initially placed in service, and verified every six months thereafter. If the value of a calibrator or calibration verification material is near that of the cut-off, then the process of calibration or calibration verification satisfies this checklist question.

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 failure of quality control to meet established criteria.

Appropriate materials for establishment and verification of the cut-off are identical to those recommended for calibration verification (listed in the introduction to the Calibration and Standards section of the Chemistry and Toxicology checklist). Note that QC materials are acceptable if the material is specifically designated by the method manufacturer as suitable for verification of the method's calibration process.

COMMENTARY:

N/A

CHM.13800

Phase II

N/A YES NO

If the laboratory uses more than one instrument to test for a given analyte, are the instruments checked against each other at least twice a year for correlation of patient/client results?

NOTE: This question applies to quantitative tests performed on the same or different instrument makes/models. This comparison must include all instruments. The use of fresh human samples (whole blood, serum, plasma, urine, etc.), rather than stabilized commercial controls, is important to directly address the issue of whether a patient/client sample yields the same results on all of the laboratory's instruments. Statistical agreement of commercial control materials across instruments does not guarantee comparability of patient/client specimen results because of potential matrix effects. In cases when pre-analytical stability of patient/client specimens is a limiting factor, alternative protocols based on QC or reference materials may be necessary but the materials used should be validated to have the same response as fresh human samples for the instruments/methods involved.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5236 [42CFR493.1281(a)]; 2) Podczasy JJ, et al. Clinical evaluation of the

Accu-Chek Advantage blood glucose monitoring system. *Lab Med.* 1997;28:462-466; 3) Ross JW, *et al.* The accuracy of laboratory measurements in clinical chemistry: a study of eleven analytes in the College of American Pathologists Chemistry Survey with fresh frozen serum, definitive methods and reference methods. *Arch Pathol Lab Med.* 1998;122:587-608.

CONTROLS

Controls are samples that act as surrogates for patient/client specimens. They are periodically processed like a patient/client sample to monitor the ongoing performance of the entire analytic process.

Most quantitative tests are traditionally monitored with 2 levels of liquid control material. This is done at a frequency within which the accuracy and precision of the measuring system is expected to be stable (typically based upon manufacturer's recommendations), but at least each day that patient/client testing is performed. The daily use of two levels of liquid control may NOT be required for certain test systems, where the daily use of instrument and/or electronic controls is demonstrably sufficient to validate that calibration status is maintained within acceptable limits.

The daily use of 2 levels of instrument and/or electronic controls as the only QC system is acceptable only for unmodified test systems cleared by the FDA and classified under CLIA-88 as "waived" or "moderately complex." The laboratory is expected to provide documentation of its validation of all instrument-reagent systems for which daily controls are limited to instrument and/or electronic controls, and the inspector will review these data to assess the adequacy of the QC system. This documentation must include the Federal complexity classification of the testing system AND data showing that calibration status is monitored.

CHM.13900**Phase II****N/A YES NO**

For QUANTITATIVE tests, are control materials at more than one concentration (level) used at least daily?

NOTE: Controls should verify assay performance at relevant decision points. The selection of these points may be based on clinical criteria, or, for certain tests (e.g., urine drugs of abuse), administrative criteria. Control testing is not necessary on days when patient testing is not performed.

The daily use of 2 levels of instrument and/or electronic controls as the only QC system is acceptable only for unmodified test systems cleared by the FDA and classified under CLIA-88 as "waived" or "moderate complexity." The laboratory is expected to provide documentation of its validation of all instrument-reagent systems for which daily controls are limited to instrument and/or electronic controls. For laboratories subject to CLIA-88, this documentation must include the Federal complexity classification of the testing system and data showing that calibration status is monitored.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5232 [42CFR493.1256(d)(3)(i)]; 2) Steindel SJ, Tetrault G. Quality control practices for calcium, cholesterol, digoxin, and hemoglobin. A College of American Pathologists Q-Probes study in 505 hospital laboratories. *Arch Pathol Lab Med*. 1998;122:401-408; 3) Voss EM, *et al*. Determining acceptability of blood glucose meters. Statistical methods for determining error. *Lab Med*. 1996;27:601-606; 4) NCCLS. Statistical quality control for quantitative measurements: principles and definitions - second edition; approved guideline C24-A2. Wayne, PA: NCCLS, 1998; 5) Ye JJ, *et al*. Performance evaluation and planning for patient/client-based quality control procedures. *Am J Clin Pathol*. 2000;113:240-248.

****REVISED**** **03/30/2005**

CHM.14000 **Phase II** **N/A YES NO**

For quantitative tests, has a valid acceptable range been established or verified for each lot of control material?

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

COMMENTARY:

N/A

REFERENCES: 1) NCCLS. Evaluation of precision performance of clinical chemistry devices; approved guideline EP5-A. Wayne, PA: NCCLS, 1998; 2) NCCLS. User demonstration of performance for precision and accuracy; approved guideline EP15-A. Wayne, PA: NCCLS, 2002; 3) Ross JW, Lawson NS. Analytic goals, concentration relationships, and the state of the art of clinical laboratory precision. *Arch Pathol Lab Med* 1995;119:495-513; 4) Steindel SJ, Tetrault G. Quality control practices for calcium, cholesterol, digoxin, and hemoglobin. A College of American Pathologists Q-Probes study in 505 hospital laboratories. *Arch Pathol Lab Med* 1998;122:401-408; 5) NCCLS. Quality Management for Unit-Use Testing; Approved Guideline. NCCLS document EP18-A (ISBN 1-56238-481-3). NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2002.

****REVISED**** **10/06/2005**

CHM.14100 **Phase II** **N/A YES NO**

For QUALITATIVE tests, is a positive and negative control included with each run of patient/client specimens?

NOTE: Controls may be liquid/external, procedural/internal, or electronic. An analytical run is the interval within which the accuracy and precision of the measuring system is expected to be stable, based upon manufacturers' instructions, and shall not exceed 24 hours. As an exception to this general practice, the specific frequency of such testing for multiparameter urine chemistry dipsticks may vary according to workload and testing location, and may not occur with each run. However, the frequency must be defined and followed by the laboratory.

For tests that report qualitative results based on a quantitative measurement using a threshold (cut-off value) to discriminate between a positive and negative clinical interpretation (for example, tests for hepatitis markers or urine drugs of abuse), the positive and negative controls must have values appropriately near the cut-off value.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7166 [42CFR493.1256(d)(3)(ii)].

CHM.14125 **Phase II** **N/A YES NO**

If the laboratory prepares calibrators and controls in-house, are these materials prepared separately?

NOTE: In general, calibrators should not be used as QC materials. If calibrators are used as controls, then different preparations should be used for these two functions.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(d)(9)].

CHM.14150**Phase II**

N/A YES NO

If a calibrator obtained from an outside supplier is used as a control, is it a different lot number from that used to calibrate the method?

NOTE: In general, calibrators should not be used as QC materials. However, this practice may be necessary for some methods when a separate control product is not available. In such cases, the calibrator used as a control must, whenever possible, be from a different lot number than that used to calibrate the method.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(d)(9)].

CHM.14200**Phase II**

N/A YES NO

If the laboratory performs test procedures for which calibration and control materials are not commercially available, have guidelines been established to verify the accuracy of patient/client test results?

COMMENTARY:

N/A

CHM.14300**Phase II**

N/A YES NO

Are quality control data organized and presented so they can be evaluated daily by the technical staff to detect problems, trends, etc.?

NOTE: Results of controls must be recorded or plotted to readily detect a malfunction in the instrument or in the analytic system. These control records must be readily available to the person performing the test.

COMMENTARY:

N/A

REFERENCE: NCCLS. Statistical quality control for quantitative measurements: principles and definitions - second edition; approved guideline C24-A2. Wayne, PA: NCCLS, 1998.

CHM.14500 **Phase II** **N/A YES NO**

For numeric QC data, are quality control statistics (e.g., SD and CV) calculated at specified intervals to define analytic imprecision?

NOTE: The laboratory must calculate imprecision statistics (e.g., SD and CV) at specified intervals for numeric QC data. For whole blood methods, where stabilized whole blood or other suitable material is not available for QC, such statistics may be generated from previous patient/client samples using the SD of duplicate pairs.

COMMENTARY:

N/A

REFERENCES: 1) Mukherjee KL. Introductory mathematics for the clinical laboratory. Chicago: American Society of Clinical Pathology, 1979:81-94; 2) Barnett RN. Clinical laboratory statistics, 2nd ed. Boston, MA: Little, Brown, 1979; 3) Weisbrodt IM. Statistics for the clinical laboratory. Philadelphia, PA: JB Lippincott, 1985; 4) Matthews DF, Farewell VT. Understanding and using medical statistics. New York, NY: Karger, 1988; 5) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7146 [42CFR493.1256(d)(10)(i)]; 6) Ross JW, Lawson NS. Analytic goals, concentrations relationships, and the state of the art for clinical laboratory precision. *Arch Pathol Lab Med*. 1995;119:495-513; 7) NCCLS. Laboratory statistics – standard deviation; a report. Wayne, PA: NCCLS, 1995; 8) NCCLS. Statistical quality control for quantitative measurements: principles and definitions - second edition; approved guideline C24-A2. Wayne, PA: NCCLS, 1998; 9) Brooks ZC, *et al*. Critical systematic error supports used of varied QC rules in routine chemistry. *Clin Chem*. 2000;46:A70.

CHM.14600 **Phase II** **N/A YES NO**

Is there documentation of corrective action when control results exceed defined tolerance limits?

NOTE: Patient/client 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.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Oct 1):1046[42CFR493.1282(b)(2)].

CHM.14800 Phase II**N/A YES NO**

Are control specimens tested in the same manner and by the same personnel as patient/client samples?

NOTE: It is implicit in quality control (QC) that control specimens are tested in the same manner as patient/client specimens. Moreover, QC specimens must be analyzed by personnel who routinely perform patient/client testing - this does not imply that each operator must perform QC daily, so long as each instrument and/or test system has QC performed at required frequencies, and all analysts participate in QC on a regular basis. To the extent possible, all steps of the testing process must be controlled, recognizing that pre-analytic and post-analytic variables may differ from those encountered with patient/clients.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7166 [42CFR493.1256(d)(8)]; 2) *ibid*, 2003(Jan 24):3708[42CFR493.1256(d)(7-8).

CHM.14900 Phase II**N/A YES NO**

Are the results of controls verified for acceptability before reporting results?

NOTE: Control results must be reviewed before reporting patient/client results. It is implicit in quality control that patient/client test results will not be reported when controls do not yield acceptable results. Controls must be run prior to reporting patient results after a change of analytically critical reagents, major preventive maintenance, or change of a critical instrument component.

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7166 [42CFR493.1256(f)]; 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):3708 [42CFR493.1256(d)(6)].

****NEW**** **04/06/2006**

CHM.14916 **Phase II** **N/A YES NO**

Are quality control data reviewed and assessed at least monthly by the laboratory director or designee?

COMMENTARY:

N/A

CHM.14933 **Phase II** **N/A YES NO**

For qualitative and semi-quantitative test systems that do NOT include built-in positive and negative controls, are known positive and negative controls tested on each day of analysis for all tests?

NOTE: Using the Summation Report, the Inspector will identify which specific tests fail to meet this requirement.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 1993(Jan 19):5232 [42CFR493.1256(d)(3)(ii)].

CHM.14966 **Phase II** **N/A YES NO**

For tests that DO include built-in positive and negative controls, is a positive and negative external control tested with each new kit lot number or different shipment of a given lot number for all qualitative or semi-quantitative tests?

NOTE: Manufacturers' recommendations must be followed. Use of daily internal controls (without daily external controls) is limited to systems classified as unmodified moderate complexity or waived under CLIA-88.

COMMENTARY:

N/A

RESULTS REPORTING

CHM.15000 Phase II N/A YES NO

Are all patient/client results reported with reference (normal) intervals or interpretations as appropriate?

NOTE: The laboratory must report reference (normal) intervals or interpretations with patient/client results, where such exist. This is important to allow proper interpretation of patient/client data. In addition, the use of high and low flags (generally available with a computerized laboratory information system) is recommended. In urine testing for drugs of abuse, listing the cut-off values for positive results is appropriate.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7162 [42CFR493.1291(d)].

CHM.15100 Phase II N/A YES NO

Are documented criteria established for immediate notification of a physician or other clinical personnel responsible for patient care when the results of certain tests exceed critical limits that are important for prompt patient management decisions ?

NOTE: Criteria for immediate notification of a physician or other clinical personnel responsible for patient care must be established for critical tests (glucose, potassium, calcium, etc.). These criteria may be indicated either in the procedure manual or in a separate policy manual. The bench technologists must be familiar with critical limits for procedures that they perform.

COMMENTARY:

N/A

REFERENCES: 1) Kost GJ. Critical limits for urgent clinician notification at US medical centers. *JAMA*. 1990;263:704-707; 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):[42CFR493.1251(b)(13)]; 3) Steindel SJ, Heard NV. Critical values: data analysis and critique. Q-Probes 92-04. Northfield, IL: College of American Pathologists, 1992; 4) Kost GJ. Using

critical limits to improve patient outcome. *Med Lab Observ.* 1993;25(3):22-27; 5) Tate KE, Gardner RM. Computers, quality, and the clinical laboratory: a look at critical values. *Proc Annu Symp Comput Appl Med Care.* 1993;193-197; 6) Kaufman HW, Collins C. Notifying clients of life-threatening results. *Med Lab Observ.* 1994;26(8):44-45; 7) Lum G. Evaluation of a laboratory critical limit (alert value) policy for hypercalcemia. *Arch Pathol Lab Med.* 1996;120:633-636; 8) Emancipator K. Critical values. ASCP practice parameter. *Am J Clin Pathol.* 1997;108:247-253; 9) Howanitz PJ, Cembrowski GS. Postanalytical quality improvement. A College of American Pathologists Q-Probes study of elevated calcium results in 525 institutions. *Arch Pathol Lab Med.* 2000;124:504-510; 10) Dalton-Beninato K. Critical value notifications are never welcome news. *Lab Med.* 2000;31:319-323; 11) Howanitz PJ, *et al.* Laboratory critical values policies and procedures. A College of American Pathologists Q-probes study in 623 institutions. *Arch Pathol Lab Med.* 2002;126:663-669; 12) Hortin GL, *et al.* Intraoperative parathyroid hormone testing. Survey of testing program characteristics. *Arch Pathol Lab Med.* 2002;126:1045-1049.

CHM.15200**Phase II****N/A YES NO**

Is there documentation of prompt notification of the physician (or other clinical personnel responsible for patient care) of results of all critical values?

NOTE: Records must be maintained indicating the prompt notification of the appropriate clinical individual after observing results in the critical range. These records should include: date, time, responsible laboratory individual, person notified and test results. In addition, the laboratory should document any failure of attempts to notify the appropriate person of critical results, and document the action taken to prevent recurrence of this problem.

COMMENTARY:

N/A

REFERENCES: 1) Kost GJ. Critical limits for urgent clinician notification at US medical centers. *JAMA.* 1990;263:704-707; 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):[42CFR493.1291(g)]; 3) Steindel SJ, Heard NV. Critical values: data analysis and critique. Q-Probes 92-04. Northfield, IL: College of American Pathologists, 1992; 4) Kost GJ. Using critical limits to improve patient/client outcome. *Med Lab Observ.* 1993;25(3):22-27; 5) Dalton-Beninato K. Critical value notifications are never welcome news. *Lab Med.* 2000;31:319-323; 6) Howanitz PJ, *et al.* Laboratory critical values policies and procedures. A College of American Pathologists Q-probes study in 623 institutions. *Arch Pathol Lab Med.* 2002;126:663-669.

CHM.15250**Phase II****N/A YES NO**

Are there documented protocols for the reporting of toxicology results?

NOTE: In addition to the requirements found in the Laboratory General Checklist, the following information must be included in toxicology reports:

1. *If appropriate, substances or classes of substances analyzed as part of the toxicology test*
2. *Specimen type*
3. *Report status for positive results (i.e., unconfirmed, confirmed or pending confirmation)*
4. *If the report includes unconfirmed screening results, a statement that such results are to be used only for medical (i.e., treatment) purposes. Unconfirmed screening results must not be used for non-medical purposes (e.g., employment testing, legal testing)*

COMMENTARY:

N/A

ANALYTIC METHODS AND PROCESSES

CHM.15300

Phase II

N/A YES NO

Are reference intervals (normal ranges) established or verified by the laboratory for the population being tested?

NOTE: Age- and sex-specific reference intervals (normal values) must be verified or established by laboratory. If a formal reference interval study is not possible or practical, then the laboratory should carefully evaluate the use of published data for its own reference ranges, and retain documentation of this evaluation.

COMMENTARY:

N/A

REFERENCES: 1) Fulwood R, *et al.* Hematological and nutritional biochemistry reference data for persons 6 months-74 years of age: United States, 1976-80. Hyattsville, MD: Dept Health and Human Services pub no (PHS) 83-1682; 2) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5231 [42CFR493. 1253(b)(1)(ii) and (b)(2)(vi)]; 3) Hicks JM, *et al.* Vitamin B12 and folate. Pediatric reference ranges. *Arch Pathol Lab Med*. 1993;117:704-706; 4) Knight JA. Laboratory issues regarding geriatric patients. *Lab Med*. 1997;28:458-461; 5) Slovacek KJ, *et al.* Use of age-specific normal ranges for serum prostate-specific antigen. *Arch Pathol Lab Med*. 1998;122:330-332; 6) Soldin S, Hicks J (eds). Pediatric reference ranges, 3rd edition. Washington, DC: American Association of Clinical Chemistry Press, 1999; 7) NCCLS. How to define and determine reference intervals in the clinical laboratory; approved guideline C28-A2. Wayne, PA:

NCCLS, 2000; 8) Katzmann JA, *et al.* Serum reference intervals and diagnostic ranges for free κ and free λ immunoglobulin light chains: relative sensitivity for detection of monoclonal light chains. *Clin Chem.* 2002;48:1437-1444; 9) Horn PS, Pesce AJ. Effect of ethnicity on reference intervals. *Clin Chem.* 2002;48:1802-1804; 10) Lahti A, *et al* Impact of subgroup prevalence on partitioning of Gaussian-distributed reference values. *Clin Chem.* 2002;48:1987-1999.

CHM.15400**Phase II****N/A YES NO**

Are results falling outside the AMR limits reviewed and reassayed if necessary before reporting?

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

Apparent analyte values that are lower or higher than the AMR do not routinely require repeat analysis if the result is reported as less than the lower limit, or greater than the upper limit, respectively, and the laboratory has evidence that the low result is not due to sampling/dilution errors, immunologic "hook effects," etc. In special cases, the procedure should state if an analyte cannot be diluted or concentrated, or if there are limitations to the amount of dilution or concentration that can be successfully used.

The CLINICALLY REPORTABLE RANGE (CRR) is the range of analyte values that a method can report as a quantitative result, allowing for specimen dilution, concentration or other pretreatment used to extend the direct AMR. For example, if it is desired to report a result that exceeds the AMR, the specimen is commonly diluted to bring the analyte into that range, the diluted specimen is reassayed, and the final result calculated using the dilution factor.

The establishment of the CRR is a medical judgment made by the laboratory director, and is based in part on the assay technology. The CRR is typically established at the time of initial method validation, and it does not need to be re-evaluated unless the methodology changes for the analyte. The method manufacturer frequently will specify the AMR and procedures to use for dilution or concentration of specimens with values outside the AMR.

The lower limit of the CRR is typically the lower limit of the AMR of the method, as verified during method validation and stated in the procedure manual. Values lower than this limit will be reported as less than the limit. The upper limit of the CRR is typically not specified unless there is a measurement limitation of a dilution protocol for an analyte. It is acceptable to dilute until a value in the AMR is achieved. The diluent should be specified for each analyte that can be successfully diluted to bring its quantity into the AMR.

An example of a CRR with both low and high limits is given for hCG as follows: Assume that the AMR is 3-1,000 mIU/mL. A laboratory director establishes that, for proper patient/client care, the CRR is 5-1,000,000 mIU/mL. The lower CRR is based on medical judgment that lower values are not diagnostic for pregnancy, while values above the upper CRR are not useful for diagnostic or prognostic purposes. Patient/client specimens with analytical measured results of <3, 3, or 4 mIU/mL are reported as "<5 mIU/mL"; specimens with analytic results >1,000 are diluted and rerun to obtain

quantitative values up to 1,000,000 mIU/mL; specimens with analytic results >1,000,000 mIU/mL are reported as ">1,000,000 mIU/mL".

An example of a CRR with only a low limit is given for aspartate aminotransferase (AST) as follows: assume the AMR is 4-900 IU/L. A laboratory director establishes that numeric values <4 are not clinically useful, while values >900 are clinically useful. Patient/client specimens with measured results of <4 are reported as "<4 IU/L"; specimens with analytic results >900 are diluted and reassayed until a quantitative result is obtained. In this case, the upper CRR is not specified because specimens are diluted until a quantitative value is obtained.

COMMENTARY:

Upper and lower limits of the analytical measurement range (AMR) for all analytes must be defined. Results that fall outside these limits must be appropriately reviewed and reassayed if necessary before reporting.

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register*. 2003(Jan 24):7164 [42CFR493.1253(a)].

CHM.15500

Phase II

N/A YES NO

Are dilution protocols and diluents (or concentration protocols) specified for all methods for which the CRR exceeds the AMR?

NOTE: When a test result exceeds the AMR, the laboratory may dilute or concentrate the specimen to adjust the analyte content to be within the AMR, then repeat the assay to obtain a quantitative result. The procedure manual must include the protocol for dilution or concentration, any diluents or other components used in the process, and the calculation of the final reportable result. If there is a limit to the amount of dilution or concentration that is appropriate for an analyte, the procedure must state the limit, and specify how to report results that exceed the CRR.

COMMENTARY:

N/A

METHODS AND INSTRUMENT SYSTEMS

must be controlled by appropriate quality control samples whose concentrations bracket the AMR. In addition, inclusion of a negative control (reagent blank) is good laboratory practice.

Calibrators or standards should be run with each analytic batch unless the system is FDA-cleared with a different calibration design.

COMMENTARY:

N/A

CHM.17300 Phase II N/A YES NO

Are appropriate controls extracted and run through the entire procedure?

NOTE: When the procedure includes an extraction step, appropriate controls must be extracted and carried through the entire procedure. Controls must include at least a negative, normal or subtherapeutic control and a positive, abnormal or therapeutic control as appropriate.

COMMENTARY:

N/A

REFERENCE: Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24):5232 [42CFR493.1256].

CHM.17500 Phase I N/A YES NO

If a hydrolysis step is required in the assay, does the laboratory include a control (when available) with each batch to evaluate the effectiveness of hydrolysis?

COMMENTARY:

N/A

CHM.17700 Phase II N/A YES NO

Are new columns verified for performance before use?

COMMENTARY:

N/A

CHM.17800 **Phase II** **N/A YES NO**

Are reagents and solvents of appropriate grade?

COMMENTARY:

N/A

CHM.17900 **Phase II** **N/A YES NO**

Are procedures documented for operation, calibration, and maintenance?

COMMENTARY:

N/A

CHM.18000 **Phase II** **N/A YES NO**

Does the documented procedure require monitoring the performance of the column and detector on each day of use?

NOTE: Unextracted standards, extracted calibrators or controls, typically containing the target compound(s), may be analyzed to monitor critical aspects of HPLC performance. Appropriate criteria for evaluating such parameters as retention time, relative retention compounds time, separation of closely eluting of interest, plates, chromatography quality and detector response should be established and monitored.

COMMENTARY:

N/A

CHM.18100 **Phase II** **N/A YES NO**

Is there a procedure for the detection of potential carryover?

NOTE: No matter what type of injection is used, the procedure must address criteria for the evaluation of potential carryover from a preceding elevated (high concentration) to the following sample in each analytical batch analysis.

COMMENTARY:

N/A

manufacturer are used, have these procedures been validated and the records maintained on file?

COMMENTARY:

N/A

CHM.18600 Phase II

N/A YES NO

Are the mass spectrometers tuned each day of patient/client testing, or according to manufacturer's recommendations and are tune records maintained?

NOTE: Acceptable tolerance limits for tune parameters must be defined, and tune records maintained.

COMMENTARY:

Mass spectrometers must be tuned either manually or automatically for each day of patient/client testing, or according to manufacturer's recommendations. The laboratory must define acceptable tolerance limits, and maintain tune records.

CHM.18700 Phase II

N/A YES NO

Are the identification criteria for single stage mass spectrometry (i.e., GC/MS, LC/MS) in compliance with recommendations?

NOTE: One acceptable criterion for compound identification by GC/MS using ion ratios is that the unknown result must have ion ratios within a prescribed acceptance or tolerance limit (e.g., $\pm 20\%$ of those of calibrators). This limit should be supported by either literature references (e.g., NCCLS 43-A for GC/MS) or through experimental means. Such ion ratio tolerance limits may differ based on the technique applied (e.g., GC/MS versus LC/MS) as well as the analyte(s) being determined (e.g., compounds with mainly ions of low abundance); thus, a defined limit to cover all methods and analytes cannot be given. In general, for LC/MS, ion ratios of $\pm 30\%$ are practical and attainable. However, consideration should be given to the relative abundance of the generated ions (see 96/23/EC 17.8.2002).

Identification using ion ratios typically requires the use of at least 2 ion ratios. However, one ion ratio of 2 characteristic ions may be acceptable if there are only a few characteristic ratios AND if there are other identifying characteristics, e.g., retention time. The internal standard's identification should be monitored with at least one ion ratio. An acceptable criterion for compound identification using total spectra is that the unknown result must have a "spectral match" quality or fit that is within the defined limits that the laboratory has set and validated. Ion ratios determined from total spectra analysis are an acceptable identification method, and should fulfill the same criteria as given above for ion ratio identification.

Laboratories using mass spectrometric methods for quantitative purposes only without ion ratios should have ancillary information and assay characteristics that validate this process, e.g., known compound of interest, retention times, potential interferences by endogenous compounds or other drugs/metabolites, etc.

COMMENTARY:

N/A

REFERENCES: 1) NCCLS. Gas chromatography/mass spectrometry (GC/MS) confirmation of drugs; approved guideline C43-A. Wayne, PA: NCCLS, 2002; 2) Official Journal of the European Communities. Commission Decision implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results (17.8.2002).

CHM.18800

Phase II

N/A YES NO

Do the identification criteria for tandem mass spectrometry (MS/MS) comply with recommendations?

NOTE: An acceptable tolerance criterion for compound identification using ion ratios is mandatory in addition to a defined number of ion ratios. Tolerance limits should accurately reflect the limitations of the method employed and should be supported by references from the literature or experimental data. For example, in GC/MS/MS, the unknown result may have prescribed ion ratio tolerances within $\pm 25\%$ of the extracted calibrator(s) (see NCCLS 43-A). In another approach for GC/MS/MS and LC/MS/MS, a two-fold acceptance criteria of data is applied whereby both tolerances for at least 3 ion ratios based on relative ion intensity (see table below) and a relative scoring system must be within prescribed limits (see 96/23/EC 17.8.2002 for details).

Relative intensity (% of base peak)	Maximum Tolerance for LC-MS ⁿ
>50%	$\pm 20\%$
>20-50%	$\pm 25\%$
>10-20%	$\pm 30\%$
$\leq 10\%$	$\pm 50\%$

Importantly, other procedures may exist. Again, each laboratory should have a method in place that is generally accepted or readily supportable.

Also note, identification using selected reaction monitoring (SRM) typically requires the use of at least one ion ratio. Where only a single ion ratio is used, other assay characteristics should be considered to strengthen the identification, e.g., retention time, control for interferences, etc. If enough ions of sufficient abundance exist, two or more ion ratios should be monitored. Identification is strengthened with a greater number of ion ratios. The internal standard's identification should be monitored with at least one ion ratio. An acceptable criterion for compound identification using total spectra is that the unknown result must have a "spectral match" quality or fit that is within the defined limits that the

laboratory has set and validated. Ion ratios determined from total spectral analysis are an acceptable identification method and should fulfill the same criteria as given above for ion ratio identifications.

Laboratories using tandem mass spectrometric methods for quantitative purposes only without ion ratios should have ancillary information and assay characteristics that validate this process, e.g., known administration of a drug to a patient, retention times, potential interferences by endogenous compounds or other drugs/metabolites, etc.

COMMENTARY:

N/A

REFERENCES: 1) NCCLS. Gas chromatography/mass spectrometry (GC/MS) confirmation of drugs; approved guideline C43-A. Wayne, PA: NCCLS, 2002; 2) Official Journal of the European Communities. Commission Decision implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results (17.8.2002).

CHM.18900

Phase II

N/A YES NO

For LC/MS, does the laboratory's assay procedure include an evaluation for possible ion-suppression?

NOTE: Ion suppression is a recognized analytical anomaly in LC/MS experiments. Such suppression can lead to false negative results or poor quantitative analyses. While difficult to predict and observe from specimen to specimen, certain precautions should be used to try to recognize when ion suppression occurs. As an example, for isotopically-labeled internal standards, if there is poor recovery of the internal standard, a signal to noise ratio greater than 3:1 should still suffice for acceptance of the specimen in question. If recovery of the isotopically-labeled internal standard is considered poor, then an alternate analysis should be considered, e.g., the method of standard addition. For analogue-type internal standards, internal standard recovery may be used as a guide for identification of ion suppression, although another option, such as the method of standard addition, would be a reasonable alternative.

COMMENTARY:

N/A

REFERENCES: 1) Annesley, T.M. Ion Suppression in Mass Spectrometry. *Clin. Chem.*, 49, pp. 1041-1044 (2003); 2) Krull, I. and Swartz, M. Quantitation in Method Validation. *LC-GC*, 16, pp. 1084-1090 (1998).

peak width, the possible interference due to copper may be mitigated or eliminated. With high resolution ICP/MS, it may be acceptable to have designated acceptable peak width range levels for different analytes.

COMMENTARY:

N/A

CHM.20600

Phase II

N/A YES NO

When appropriate, are oxides and doubly-charged species minimized?

NOTE: Oxides and doubly-charged species are common interferences in ICP/MS. Oxides of various elements may have overlapping signals with elements of the same mass, thus leading to false-positive findings. Special techniques such as high resolution ICP/MS, dynamic-reaction cell and collision-reaction cell processes may eliminate the concern for oxide interference. Elements with a second ionization potential greater than or equal to 15.8 eV (the ionization potential of argon) may be doubly-charged. Such doubly-charged species may suggest the presence of an element that is not truly present. For example, gadolinium has an isotope at m/e154. It has a doubly-charged species at m/e 77, which is also the same mass as an isotope of selenium, as well as a mass used as a correction factor for arsenic interference by ArCl³⁷. Despite the potential for a doubly-charged species, if the analyte of interest cannot be interfered with by known doubly-charged species, then such concern is unwarranted.

COMMENTARY:

N/A

CHM.20700

Phase II

N/A YES NO

If the dual detector mode is applied, is the calibration verified?

NOTE: In ICP/MS, calibration can be performed in two modes – pulse counting for lower concentrations and analog for higher concentrations. If a range is necessary that overlaps with both modes, then the laboratory should employ a cross-calibration. This is generally accomplished by use of a tuning solution whereby a full calibration is performed in both modes followed by software adjustment for a smooth transition. If a concentration range is needed that only encompasses one mode or the other, then a cross-calibration is unnecessary as long as the appropriate mode is employed.

COMMENTARY:

N/A

NOTE: When isotopes and internal standards are measured by ICP/MS, interferences (isobaric and polyatomic species) and relative abundances must be considered and described in written procedures and/or assay validation materials.

COMMENTARY:

N/A

CHM.21200 Phase I N/A YES NO

Are mechanisms in place to minimize and detect contamination of results obtained by ICP/MS?

NOTE: Potential sources of contamination that should be evaluated and managed in an ICP/MS laboratory include specimen collection, reagent handling, carryover between samples, and engineering controls within the analytical environment.

COMMENTARY:

N/A

CHM.21300 Phase I N/A YES NO

Is the purity of each gas and reagent used with ICP/MS defined, documented, and appropriate for the intended use?

NOTE: Purity of gasses and reagents (including water) used with ICP/MS should be defined and validated to identify and minimize interferences and sources of contamination.

COMMENTARY:

N/A

CHM.21400 Phase I N/A YES NO

Are controls, calibrators, and blanks matrix-matched to the sample type?

NOTE: The matrices of controls, calibrators, and blanks may affect the ions generated and should be considered in the design and validation of each ICP/MS assay. If matrices are not an issue,, the laboratory should have documented that matrix-matching is not necessary.

COMMENTARY:

N/A

CHM.21900 **Phase II** **N/A YES NO**

Are automatic sampler systems (e.g., on graphite furnace) checked for precision at specified periodic intervals?

COMMENTARY:

N/A

CHM.22000 **Phase II** **N/A YES NO**

If a graphite furnace is used, is the blank value of a graphite tube verified for each element tested?

NOTE: Residue from assayed samples may accumulate on the graphite tube, thus potentially resulting in false positive findings should the residue contain the element of interest. In addition, checking for the response of a blank may also serve as one of the indicators that the graphite tube may need replacement.

COMMENTARY:

N/A

CHM.22100 **Phase II** **N/A YES NO**

Is an adequate and appropriate calibration curve established for quantitative testing?

COMMENTARY:

N/A

CHM.22200 **Phase II** **N/A YES NO**

Is the lamp's energy verified and recorded for each run?

NOTE: Atomic absorption spectrophotometric lamp energy must be verified and recorded for each run. Lamps lose performance characteristics over time. Decrements in lamp performance may be observed by a loss of sensitivity. Poor lamp performance may also serve as an indicator of another system failure, e.g., loose connections.

COMMENTARY:

N/A

.....
Colorimeters and Spectrophotometers
.....

CHM.22300 Phase II N/A YES NO

Are absorbance and linearity checked periodically with filters or standard solutions, if required by the instrument manufacturer?

COMMENTARY:

N/A

CHM.22400 Phase II N/A YES NO

Is the spectrophotometer wavelength calibration checked regularly with appropriate solutions, filters or emission line source lamps, (if required by the instrument manufacturer), and are the results documented?

COMMENTARY:

N/A

CHM.22500 Phase II N/A YES NO

Is stray light checked periodically with extinction filters or appropriate solutions, if required by the instrument manufacturer?

COMMENTARY:

N/A

CHM.22600 Phase II N/A YES NO

For procedures using calibration curves, are all the curves rerun regularly and/or verified after servicing or recalibration of instruments?

COMMENTARY:

N/A

responsible for the reliability and proper function of their instruments and must have access to this information. Off-site storage, such as with centralized medical maintenance or computer files, is not precluded if the inspector is satisfied that the records can be promptly retrieved.

COMMENTARY:

N/A

.....
Glassware
.....

CHM.23800**Phase II****N/A YES NO**

Are glass volumetric flasks of certified accuracy (Class A, National Institute of Standards and Technology (NIST) Standard or equivalent) or if non-certified volumetric glassware is used, are all items checked for accuracy of calibration before initial use?

COMMENTARY:

N/A

CHM.23900**Phase II****N/A YES NO**

Are glass volumetric pipettes of certified accuracy (Class A); or are they checked by gravimetric, colorimetric, or some other verification procedure before initial use?

NOTE: The following Table shows the American Society for Testing and Materials' calibration (accuracy) specifications for Class A volumetric pipettes:

<i>Nominal Capacity (mL)</i>	<i>Variation (\pm mL)</i>
<i>0.5 - 2</i>	<i>0.006</i>
<i>3 - 7</i>	<i>0.01</i>
<i>8 - 10</i>	<i>0.02</i>
<i>15 - 30</i>	<i>0.03</i>
<i>40 - 50</i>	<i>0.05</i>
<i>100</i>	<i>0.08</i>

Reconstitution of lyophilized calibrators, controls, or proficiency testing materials, or any other tasks requiring accurate volumetric measurement, must be performed only with measuring devices of Class A accuracy, or those for which accuracy has been defined and deemed acceptable for the intended use.

COMMENTARY:

N/A

REFERENCES: 1) Curtis RH. Performance verification of manual action pipets. Part I. *Am Clin Lab.* 1994;12(7):8-9; 2) Curtis RH. Performance verification of manual action pipets. Part II. *Am Clin Lab.* 1994;12(9):16-17; 3) Perrier S, *et al.* Micro-pipette calibration using a ratiometric photometer-reagent system as compared to the gravimetric method. *Clin Chem.* 1995;41:S183; 4) American Society for Testing and Materials. Standard specification for glass volumetric (transfer) pipets, designation E 969-95. Philadelphia, PA: ASTM, 1995; 5) Johnson B. Calibration to dye for: Artel's new pipette calibration system. *Scientist.* 1999;13(12):14; 6) Connors M, Curtis R. Pipetting error: a real problem with a simple solution. Parts I and II. *Am Lab News.* 1999;31(13):20-22; 7) Skeen GA, Ashwood ER. Using spectrophotometry to evaluate volumetric devices. *Lab Med.* 2000;31:478-479.

CHM.24000

Phase II

N/A YES NO

Are non-class A pipettes that are used for quantitative dispensing of material checked for accuracy and reproducibility at specified intervals, and results documented?

NOTE: Such checks are most simply done gravimetrically. This consists of transferring a number of measured samples of water from the pipette to a balance. Each weight is recorded, the weights are converted to volumes, and then means (for accuracy), and SD/CV (for imprecision) are calculated. Alternative approaches include spectrophotometry or (less frequently) the use of radioactive isotopes, and commercial kits are available from a number of vendors. Computer software is useful where there are many pipettes, and provides convenient documentation.

COMMENTARY:

N/A

REFERENCES: 1) Curtis RH. Performance verification of manual action pipets. Part I. *Am Clin Lab.* 1994;12(7):8-9; 2) Curtis RH. Performance verification of manual action pipets. Part II. *Am Clin Lab.* 1994;12(9):16-17; 3) Perrier S, *et al.* Micro-pipette calibration using a ratiometric photometer-reagent system as compared to the gravimetric method. *Clin Chem.* 1995;41:S183; 4) Bray W. Software for the gravimetric calibration testing of pipets. *Am Clin Lab.* Oct 1995 (available on the internet at http://www.labtronics.com/pt_art.htm); 5) Kroll MH, *et al* (eds). Laboratory instrument evaluation, verification & maintenance manual, 5th edition. Northfield, IL: College of American Pathologists, 1999:126-127; 6) Johnson B. Calibration to dye for: Artel's new pipette calibration system. *Scientist.* 1999;13(12):14; 7) Connors M, Curtis R. Pipetting error: a real problem with a simple solution. Parts I and II. *Am Lab News.* 1999;31(13):20-22; 8) Skeen GA, Ashwood ER. Using spectrophotometry to evaluate volumetric devices. *Lab Med.* 2000;31:478-479.

****REVISED**** **03/30/2005**

CHM.24100 **Phase I** **N/A YES NO**

Is the use of less precise measuring devices such as serological plastic pipettes and graduated cylinders limited to situations where the accuracy and precision of calibrated glass pipettes are not required?

NOTE: In contrast with the more stringent accuracy requirements of glass pipettes, ASTM requirements for plastic pipettes are $\pm 3\%$ of the stated volume. The procedure manual should specify when the use of non-class A measuring devices is permissible.

COMMENTARY:

N/A

REFERENCE: American Society for Testing and Materials. Standard specification for serological pipets, disposable plastic, designation E 934-88, In 1993 Annual Book of ASTM Standards, section 14 (general methods and instrumentation). Philadelphia, PA: ASTM, 1993:14.02:485-486.

.....
Automatic Pipettes - Fixed Volume Adjustable and/or Micropipettes

.....
Automatic pipettes and diluting devices of all types must be checked for accuracy and reproducibility before being placed in service and periodically thereafter.

CHM.24200 **Phase II** **N/A YES NO**

Is there a documented procedure defining how pipettes are checked for accuracy of calibration (gravimetric, colorimetric, volumetric or other verification procedure) before being placed in service initially, and results documented?

NOTE: Automatic pipettes (fixed volume adjustable and/or micropipettes) must be checked for calibration accuracy either by volumetric, colorimetric, gravimetric, or other means before being placed in service initially, and results documented.

COMMENTARY:

N/A

REFERENCES: 1) Curtis RH. Performance verification of manual action pipets. Part I. *Am Clin Lab.* 1994;12(7):8-9; 2) Curtis RH. Performance verification of manual action pipets. Part II. *Am Clin Lab.* 1994;12(9):16-17; 3) Perrier S, *et al.* Micro-pipette calibration using a ratiometric photometer-reagent system as compared to the gravimetric method. *Clin Chem.* 1995;41:S183; 4) Bray W. Software for the gravimetric calibration testing of pipets. *Am Clin Lab.* Oct 1995 (available on the internet at http://www.labtronics.com/pt_art.htm); 5) Kroll MH, *et al* (eds). Laboratory instrument evaluation, verification & maintenance manual, 5th edition. Northfield, IL: College of American Pathologists, 1999:126-127; 6) Johnson B. Calibration to dye for: Artel's new pipette calibration system. *Scientist.* 1999;13(12):14; 7) Connors M, Curtis R. Pipetting error: a real problem with a simple solution. Parts I and II. *Am Lab News.* 1999;31(13):20-22; 8) Skeen GA, Ashwood ER. Using spectrophotometry to evaluate volumetric devices. *Lab Med.* 2000;31:478-479.

CHM.24300**Phase II****N/A YES NO**

Are automatic pipettes used for quantitative dispensing checked for accuracy and reproducibility (gravimetric, colorimetric or other verification procedure) at specified, periodic intervals, and are the results recorded?

NOTE: For analytic instruments with integral automatic pipettors, the accuracy and precision of the pipetting system should be checked periodically, unless that is not practical for the end-user laboratory. Manufacturers' recommendations should be followed.

COMMENTARY:

N/A

REFERENCES: 1) Curtis RH. Performance verification of manual action pipets. Part I. *Am Clin Lab.* 1994;12(7):8-9; 2) Curtis RH. Performance verification of manual action pipets. Part II. *Am Clin Lab.* 1994;12(9):16-17; 3) Perrier S, *et al.* Micro-pipette calibration using a ratiometric photometer-reagent system as compared to the gravimetric method. *Clin Chem.* 1995;41:S183; 4) Bray W. Software for the gravimetric calibration testing of pipets. *Am Clin Lab.* Oct 1995 (available on the internet at http://www.labtronics.com/pt_art.htm); 5) Kroll MH, *et al* (eds). Laboratory instrument evaluation, verification & maintenance manual, 5th edition. Northfield, IL: College of American Pathologists, 1999:126-127; 6) Johnson B. Calibration to dye for: Artel's new pipette calibration system. *Scientist.* 1999;13(12):14; 7) Connors M, Curtis R. Pipetting error: a real problem with a simple solution. Parts I and II. *Am Lab News.* 1999;31(13):20-22; 8) Skeen GA, Ashwood ER. Using spectrophotometry to evaluate volumetric devices. *Lab Med.* 2000;31:478-479.

CHM.24400**Phase II****N/A YES NO**

Has the laboratory evaluated its automatic pipetting systems for carryover?

NOTE: The laboratory must have procedures in place for evaluating whether carryover effects are present. This question applies to both stand-alone pipette systems and to sample pipettes integrated with analytic instruments.

In practice, carryover is a problem only for analytes with a wide clinical range of analyte concentration, such that a minute degree of carry-over could have significant clinical implications. Examples include immunoassays such as β-HCG, certain enzymes (e.g., CK), and certain drugs of abuse (e.g., benzoylecgonine [cocaine metabolite], which may be present in high concentrations). The laboratory should select representative examples of such analytes for carryover studies.

Evaluation for carryover is not required for automatic pipettes that use disposable tips.

One suggested method to study carryover is to run known high patient samples, followed by known low samples to see if the results of the low-level material are affected. If carryover is detected, the laboratory must determine the analyte concentration above which subsequent samples may be affected, and define this value in the procedure. Results of each analytical run must be reviewed to ensure that no results exceed this level. If results that exceed the defined level are detected, then the appropriate course of action must be defined (repeat analysis of subsequent samples, for example).

Carryover studies must be performed, as applicable, as part of the initial evaluation of an instrument. (The laboratory may use the data from carryover studies performed by instrument manufacturers, as appropriate.) It is recommended that carryover studies be repeated periodically thereafter, particularly after major maintenance or repair.

COMMENTARY:

N/A

REFERENCE: NCCLS. Preliminary evaluation of quantitative clinical laboratory methods – second edition; approved guideline EP10-A2. Wayne, PA: NCCLS, 2002.

.....

Thermometers

.....

CHM.24500

Phase II

N/A YES NO

Is an appropriate thermometric standard device of known accuracy (NIST-certified or guaranteed by manufacturer to meet NIST Standards) available?

NOTE: Thermometers should be present on all temperature-controlled instruments and environments and checked daily. Thermometric standard devices should be recalibrated or recertified prior to the date of expiration of the guarantee of calibration.

COMMENTARY:

N/A

CHM.24600 Phase II

N/A YES NO

Are all non-certified thermometers in use checked against an appropriate thermometric standard device before initial use?

COMMENTARY:

N/A

.....
Temperature-Dependent Equipment
.....

CHM.24700 Phase II

N/A YES NO

Are temperatures checked and recorded appropriately for the following types of equipment?

- 1. Water baths**
- 2. Dry baths (heating blocks)**
- 3. Instrument components (water baths, dialyzers, heating baths)**
- 4. Incubators and ovens (where temperature control is necessary for a procedure)**
- 5. Refrigerators and freezers**

NOTE: Temperature-dependent equipment containing reagents and patient/client specimens must be monitored daily, as equipment failures could affect accuracy of patient/client test results. Items such as water baths and heat blocks used for procedures need only be checked on days of patient/client testing..

COMMENTARY:

N/A

CHM.24800 Phase II

N/A YES NO

Have acceptable ranges been defined for all temperature -dependent equipment?

COMMENTARY:

N/A

CHM.24900 Phase II

N/A YES NO

Is there evidence of corrective action taken if acceptable temperature ranges for refrigerators and/or freezers are exceeded, including evaluation of contents for adverse effects?

NOTE: If acceptable temperature ranges for refrigerators and/or freezers are exceeded, reagents, controls, calibrators, etc. must be evaluated for possible adverse effects, with documentation of results.

COMMENTARY:

N/A

.....

Centrifuges

.....

CHM.25000 Phase II

N/A YES NO

Are all centrifuges used in the laboratory clean and properly maintained?

COMMENTARY:

N/A

CHM.25100 Phase II

N/A YES NO

Is there a documented protocol and schedule for maintenance of all centrifuges (cleaning, changing brushes, etc.)?

COMMENTARY:

N/A

CHM.25200 Phase II

N/A YES NO

Are the operating speeds of all centrifuges checked periodically as needed for the intended use, and is this done in a safe manner?

There are three general types of balances in use. First, many contemporary balance designs use force transducers of various designs to provide mass readings. These balances typically have built-in certified calibration weights that are utilized automatically each time of use. The second type of balance employs a force transducer design that uses external weights for calibration each time the balance is used. Typically a single mass at the maximum weighing range, in conjunction with a zero point for the pan, is used for calibration of a force transducer balance design. The third type of balance, an older design, is a mechanical balance beam with internal moveable or external calibration weights. This design may have an electronic read-out.

In all cases, verification of accuracy over the weighing range with external calibrated masses is required on a periodic schedule appropriate to the use of the balance. Balances must be checked at least every 6 months if used for weighing out materials to make up standard solutions for method calibration. For other purposes, annual verification may be adequate. Accuracy must be verified when a new balance is installed and whenever a balance is moved.

External validation of accuracy requires the appropriate class of ASTM specification weights. ASTM Class 1 weights are appropriate for calibrating high precision analytical balances (0.01 to 0.1 mg limit of precision). ASTM Class 2 weights are appropriate for calibrating precision top-loading balances (0.001 to 0.01 g precision).w ASTM Class 3 weights are appropriate for calibrating moderate precision balances, (0.01 to 0.1 g precision).

Periodic external validation of accuracy is required to ensure that internal weights have not deteriorated from adsorption of surface film or corrosion; and to ensure that electronics remain correctly calibrated.

COMMENTARY:

N/A

REFERENCES: 1) American Society for Testing and Materials. Standard specification for laboratory weights and precision mass standards, designation E 617-97 (Reapproved 2003). ASTM International, West Conshohocken, PA 19428-2959 (www.astm.org); 2) American Society for Testing and Materials. E 898-88 (Reapproved 2000). Standard method of testing top-loading, direct reading laboratory scales and balances. ASTM International, West Conshohocken, PA 19428-2959 (www.astm.org).

CHM.25600

Phase II

N/A YES NO

Are results of periodic accuracy checks recorded?

NOTE: Mass readings should be recorded in a log book. The deviations in log book readings should be no more than the precision required in the applications for which the balance is used. Acceptable ranges for readings should be specified.

COMMENTARY:

N/A

CHM.25700 Phase II

N/A YES NO

Are weights well-maintained (clean, in a covered container, not corroded) and are appropriate lifting or handling devices available?

NOTE: Weights must be well-maintained (covered when not in use, not corroded) and only be handled by devices that will not allow residual contaminants to remain on the masses. Certified masses will only meet their specifications if maintained in pristine condition.

COMMENTARY:

N/A

PERSONNEL

CHM.25800 Phase II

N/A YES NO

Does the person in charge of technical operations in chemistry have education and experience equivalent to an MT(ASCP) and at least 4 years experience (one of which must be in clinical chemistry) under a qualified director?

COMMENTARY:

N/A

CHM.25900 Phase II

N/A YES NO

Does the person in charge of technical operations in toxicology have education and experience equivalent to an MT(ASCP) or a Bachelor's degree in chemistry/biology/toxicology, and at least 4 years experience (one of which must be in toxicology) under a qualified director?

COMMENTARY:

N/A

CHM.25950 Phase II

N/A YES NO

Does the person in charge of technical operations in the blood gas section have education and experience equivalent to an MT(ASCP) (or certified or registered respiratory therapist) and at least 4 years experience (one of which must be in blood gas testing) under a qualified director?

COMMENTARY:

N/A

PHYSICAL FACILITIES

Sufficient space and utilities need to be provided for the overall workload of the automated chemistry section, and to meet all safety requirements.

CHM.26000 Phase I

N/A YES NO

Is there adequate space for administrative functions?

COMMENTARY:

N/A

CHM.26100 Phase I

N/A YES NO

Is there adequate space for clerical work?

COMMENTARY:

N/A

CHM.26200 Phase I

N/A YES NO

Is there adequate space for technical work (bench space)?

COMMENTARY:

N/A

CHM.26300 Phase I N/A YES NO

Is there adequate space for instruments?

COMMENTARY:

N/A

CHM.26400 Phase I N/A YES NO

Is there adequate space for shelf storage?

COMMENTARY:

N/A

CHM.26500 Phase I N/A YES NO

Is there adequate refrigerator/freezer storage space?

COMMENTARY:

N/A

CHM.26600 Phase I N/A YES NO

Is the available space efficiently utilized?

COMMENTARY:

N/A

CHM.26700 Phase I N/A YES NO

Is there adequate space for radionuclide storage?

NOTE: If RIAs are not performed, mark this question "N/A."

COMMENTARY:

N/A

CHM.26800 **Phase II** **N/A YES NO**

Is sufficient space available so that there is no compromise of the quality of work, (including quality control activities) or safety of personnel?

COMMENTARY:

N/A

CHM.26900 **Phase I** **N/A YES NO**

Are floors and benches clean, free of clutter and well-maintained?

COMMENTARY:

N/A

CHM.27000 **Phase I** **N/A YES NO**

Are water taps, sinks, and drains adequate for the workload of the laboratory?

COMMENTARY:

N/A

CHM.27200 **Phase I** **N/A YES NO**

Are electrical outlets adequate for the workload of the laboratory?

COMMENTARY:

N/A

CHM.27300 **Phase I** **N/A YES NO**

Is ventilation adequate for the workload and types of procedures performed in the laboratory?

COMMENTARY:

N/A

CHM.28100 **Phase I** **N/A YES NO**

Are there specific policies regarding authorization or restriction of personnel handling radionuclides?

NOTE: These policies should be incorporated into the department's radiation safety manual.

COMMENTARY:

N/A

CHM.28200 **Phase II** **N/A YES NO**

Do policies include procedures for notification if a damaged or leaking radionuclide shipment is received?

NOTE: Procedures must include inspection, monitoring of shipments, and instructions for notification, if leakage or damage is noted in a radionuclide shipment. For U.S. laboratories, this is a Department of Transportation requirement.

COMMENTARY:

N/A

REFERENCES: 1) NCCLS. *Clinical Laboratory Safety; Approved Guideline? Second Edition*. NCCLS document GP17-A2 [ISBN 1-56238-530-5]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004; 2) Department of Transportation, Research and Special Programs Administration. Hazardous materials table, special provisions, hazardous materials communications, emergency response information and training requirements. *Fed Register*. 2003 (Oct 1) [49CFR172.403, 600, 602, 604].

CHM.28300 **Phase II** **N/A YES NO**

Are radionuclide storage and decay areas properly shielded, if required for specific isotopic materials?

NOTE: Radionuclide storage and decay areas must be properly shielded, if required for specific isotopic materials, to avoid excessive exposure to personnel and interference with counting procedures.

COMMENTARY:

N/A

CHM.28700

Phase II

N/A YES NO

Is radioactive waste kept separate from normal trash, stored, and appropriately discarded with documentation?

NOTE: For U.S. laboratories, NRC regulations specify that separate areas be established for the receipt of radioactive waste and that these areas be properly shielded to reduce radiation levels below those maximum permissible limits specified in 10CFR20. Documentation of the radioactive trash disposal must be maintained.

COMMENTARY:

N/A

CHM.28800

Phase II

N/A YES NO

Is there evidence that a laboratory representative is a member of and/or attends institutional radiation safety committee meetings regularly?

NOTE: Independent laboratories must have a radiation safety officer who fulfills the functions of an institutional radiation safety committee.

COMMENTARY:

N/A

#####

GENERAL CHEMISTRY

#####

CHEMISTRY

THERAPEUTIC DRUG MONITORING

CHM.28900**Phase I****N/A YES NO**

Where such information is important, has the laboratory provided information to clinical personnel of the optimal specimen collection time in relation to drug dosing?

COMMENTARY:

N/A

REFERENCES: 1) Nicholson PW, *et al.* Ideal sampling time for drug assays. *Br J Clin Pharm.* 1980;9:467-470; 2) NCCLS. Development of requisition forms for therapeutic drug monitoring and/or overdose toxicology; approved guideline T/DM1-A. Wayne, PA: NCCLS, 1991; 3) Howanitz PJ, Steindel SJ. Digoxin therapeutic drug monitoring practices. A College of American Pathologists Q-Probes study of 666 institutions and 18679 toxic levels. *Arch Pathol Lab Med.* 1993;117:684-690; 4) Schoenenberge RA, *et al.* Appropriateness of antiepileptic drug level monitoring. *JAMA.* 1995;274:1622-1626; 5) Williamson KM, *et al.* Digoxin toxicity: an evaluation in current clinical practice. *Arch Intern Med.* 1998;158:2444-2499.

CHM.29000**Phase II****N/A YES NO**

Where applicable, are TDM results reported in relation to patient dosing and/or timing information?

NOTE: The intent is to have a mechanism whereby the clinician can easily and accurately link TDM results from the laboratory to the dosage and time of drug administration. Ideally, the test result, dose and administration time would be reported in juxtaposition on the patient chart. This may be the responsibility of the laboratory, or an integrating function of reported laboratory analytic data with clinical information from other sources.

COMMENTARY:

N/A

REFERENCES: 1) Elin RJ. Computer-assisted therapeutic drug monitoring. *Clin Lab Med.* 1987;7:485-492; 2) Howanitz PJ, Steindel SJ. Digoxin therapeutic drug monitoring practices. A College of American Pathologists Q-Probes study of 666 institutions and 18679 toxic levels. *Arch Pathol Lab Med.* 1993;117:684-690; 3) Schoenenberge RA, *et al.* Appropriateness of antiepileptic drug level monitoring. *JAMA.* 1995;274:1622-1626; 4) Williamson KM, *et al.* Digoxin toxicity: an evaluation in current clinical practice. *Arch Intern Med.* 1998;158:2444-2499; 5) Steele BW, *et al.* An evaluation of analytic goals for assays of drugs. A College of American Pathologists therapeutic drug monitoring survey study. *Arch Pathol Lab Med.* 2001;125:729-735.

NOTE: The procedures for disinfection of sweat collection equipment and facilities should be reviewed annually to assure their continued effectiveness. One suggested approach is annual evaluation by the infection control department of the institution.

COMMENTARY:

N/A

CHM.29200

Phase II

N/A YES NO

Is the laboratory following generally accepted procedures for sweat collection and analysis, including steps to minimize sample evaporation or contamination?

NOTE: Because sample evaporation and contamination can have significant impact on the validity of test results, laboratories must incorporate the following steps into their procedure and/or follow manufacturer's recommendations:

A. When using gauze or filter paper collection pads:

- 1. Use gauze and/or filter paper that is low in electrolyte content*
- 2. Wash the patient's skin thoroughly with distilled or deionized water, then dry before stimulation. Repeat after stimulation and before collection*
- 3. Do not touch the weighing vial, wax film, collection site, or collection pad. Always use forceps or powder-free gloves*
- 4. Use two pieces of waterproof adhesive tape on all sides of the paraffin wax film or wrap with a disposable stretch bandage to produce an airtight seal*
- 5. Blot back into the collection pad any condensate that may have formed on the wax film during collection. Failure to collect the condensate can result in false positive test results*
- 6. After collection, quickly transfer the specimen pad to the weighing vial and reweigh promptly*

B. When collecting sweat into macroduct coils:

- 1. Wash the patient's skin thoroughly with distilled, deionized water, then dry before stimulation. Repeat after stimulation and before collection*
- 2. Avoid touching the collecting surface of the coil*
- 3. Fasten the collector to the extremity with firm strap pressure. Test for proper attachment after sweat appears in the coils*
- 4. Do not attempt to remove the entire collector assembly from the patient's extremity before separating the coil from the main body. Loss of specimen may occur*
- 5. Do not contaminate the nippers or sweat dispensing needle with sweat sample*

C. When collecting and analyzing sweat using the Nanoduct system:

1. Wash the patient's skin thoroughly with distilled, deionized water, then dry before stimulation. Repeat after stimulation and before collection
2. Avoid touching the collecting surface of the device

COMMENTARY:

N/A

REFERENCES: 1) Scott MG, *et al.* Electrolytes and blood gases, In Burtis C and Ashwood E (eds), Tietz textbook of clinical chemistry. Philadelphia: WB Saunders, 3rd edition, 1998; 2) NCCLS. Sweat testing: sample collection and quantitative analysis; approved guideline C34-A2. Wayne, PA: NCCLS, 2000.

****REVISED**** 03/30/2005

CHM.29300 Phase II N/A YES NO

Does the protocol require sweat stimulation and collection only on the patient's lower arm or upper leg, using a site that is free from diffuse inflammation or rash?

NOTE: The protocol must require that sweat is stimulated and collected from the patient's lower arm or upper leg. Sweat must not be stimulated or collected from the head or trunk. Sweat must not be stimulated or collected from an area of diffuse inflammation, such as a rash or eczematous lesion, because of the likelihood of contamination by serous fluid.

COMMENTARY:

N/A

REFERENCES: 1) Liebke C, *et al.* Sweat electrolyte concentrations in children with atopic dermatitis. *Lancet.* 1997;350:1678; 2) NCCLS. Sweat testing: sample collection and quantitative analysis; approved guideline C34-A2. Wayne, PA: NCCLS, 2000.

CHM.29400 Phase II N/A YES NO

If the laboratory prepares the pilocarpine solution for iontophoresis, is the source of the pilocarpine U.S.P. grade or equivalent?

COMMENTARY:

N/A

CHM.29500 **Phase II** **N/A YES NO**

Does the protocol require that the electrodes used for stimulation are placed such that iontophoretic current never crosses the patient's trunk?

NOTE: The protocol must specify that electrodes used for stimulation be placed so that current does not cross the trunk, to avoid the possibility of current crossing the heart, resulting in cardiac depolarization.

COMMENTARY:

N/A

CHM.29600 **Phase II** **N/A YES NO**

Does the protocol specify the conditions of iontophoresis?

NOTE: For safety reasons, the iontophoretic current source must be battery-powered, to avoid the possibility of patient exposure to line voltage. For manually controlled devices, iontophoresis must be performed for no more than 5 min at a current less than 4 mA, to prevent burns. The iontophoresis unit must undergo a documented, regular maintenance procedure by qualified personnel (such as engineering personnel) for current leakage and current control.

COMMENTARY:

N/A

CHM.29700 **Phase II** **N/A YES NO**

Does the protocol specify that iontophoresis is withheld from patients receiving oxygen by an open delivery system?

NOTE: While the possibility of an explosion due to the generation of an electrical spark is remote, it cannot be ignored. Often, these patients can temporarily receive oxygen via a facemask or nasal cannula, in which case sweat testing can be done.

COMMENTARY:

N/A

CHM.29800**Phase II****N/A YES NO**

Does the protocol specify that the area of iontophoretic stimulation is equivalent to the area of sweat collection?

NOTE: The protocol must specify that the area of iontophoretic stimulation is equivalent to the area of sweat collection. Sweat electrolyte concentration is related to sweat rate. At low sweat rates, sweat electrolyte concentration decreases. The average sweat rate should exceed 1 g/m²/min.

To ensure adequate sweat stimulation and accurately reflect sweat electrolyte concentration, a minimum acceptable sweat volume or weight is required. This requirement is based on the size of the electrode and stimulation area, the type and size of collecting media, and the duration of sweat collection. To standardize the process, the stimulation and collection area should be equivalent, and the time of collection consistent. For example, for the positive electrode, use a 1 ½ inch x 1 ½ inch electrode over a 2 x 2 inch gauze pad saturated with pilocarpine for stimulation, then collect sweat onto a 2 x 2 inch pre-weighed gauze pad.

COMMENTARY:

N/A

REFERENCE: National Committee for Clinical Laboratory Standards. Sweat testing: sample collection and quantitative analysis; approved guideline C34-A2. Wayne, PA: NCCLS, 2000.

CHM.29850**Phase II****N/A YES NO**

Is the sweat collection device appropriate for the iontophoresis system?

NOTE: The sweat collection device must be designed for use with the appropriate iontophoresis system so that the stimulation and collection area are equivalent and the appropriate minimum acceptable sweat volume or weight can be achieved. Examples of acceptable combinations include:

- a. *Stimulation with Wescor Pilogel iontophoresis and collection into Wescor Macroduct coils*
- b. *Stimulation with copper electrodes over gauze/filter paper pilocarpine pads and collection into gauze/filter paper*
- c. *Stimulation and collection into Wescor Nanoduct conductivity cell*

Examples of unacceptable combinations include:

- a. *Stimulation with Wescor Pilogel iontophoresis and collection into gauze/filter paper*
- b. *Stimulation with Polychrome iontophoresis and collection into Wescor Macroduct coils, gauze or filter paper*
- c. *Stimulation with copper electrodes over gauze/filter paper pilocarpine pads and collection into Wescor Macroduct coils*

COMMENTARY:

N/A

REFERENCES: 1) National Committee for Clinical Laboratory Standards. Sweat testing: sample collection and quantitative analysis; approved guideline C34-A2. Wayne, PA: NCCLS, 2000; 2) Cystic Fibrosis Foundation Center Accreditation Guidelines. Bethesda, MD, 2004.

CHM.29900**Phase II****N/A YES NO****Does the protocol specify that sweat collection time may not exceed 30 minutes?**

NOTE: Extending the collection time will not significantly increase the sweat yield and may lead to sample evaporation. Samples may be taken from less than maximally stimulated glands. This may lead to a false-negative result. In addition, altering the collection time will affect the minimum acceptable sweat weight or volume, because the time parameter of the rate equation has been changed.

COMMENTARY:

N/A

CHM.30000**Phase II****N/A YES NO****Does the protocol specify the parameters of sweat collection?**

NOTE: These must include an established minimum acceptable sweat volume or weight based on the area of stimulation, area of collection and standardized time for collection. The average sweat rate should exceed 1 g/m²/min, which in general corresponds to a minimum sample weight of about 75 mg of sweat collected on a 2x2 inch gauze or filter paper and about 15 uL of sweat collected in macroduct coil in 30 min. Samples less than the required volume or weight must not be analyzed.

COMMENTARY:

N/A

REFERENCES: 1) Hjelm M, *et al.* Sweat sodium related to amount of sweat after sweat test in children with and without cystic fibrosis. *Acta Paediatr Scand.* 1986;75:652-656; 2) NCCLS. Sweat testing: sample collection and quantitative analysis; approved guideline C34-A2. Wayne, PA: NCCLS, 2000.

CHM.30100 **Phase II** **N/A YES NO**

Does the protocol specify that multiple insufficient sweat samples are rejected and not pooled for analysis?

NOTE: The laboratory must reject individual samples that do not meet minimum sample size requirements. The average sweat rate of 1 g/m²/min is determined independently for each site. The requirement is a physiologic one, not an analytic one. Samples less than the required volume or weight must not be pooled to achieve the weight/volume requirement. Measurement on samples from less than maximally stimulated sweat glands may lead to false-negative results.

COMMENTARY:

N/A

****NEW**** **03/30/2005**

CHM.30150 **Phase I** **N/A YES NO**

Is the incidence of insufficient sweat samples routinely monitored?

NOTE: Laboratories should collect data on the number of patients from whom a sufficient sweat sample has not been obtained. For patients older than 3 months of age, the annual insufficient rate should not exceed 5%. If the rate is greater than 5% the collection procedure should be reevaluated for consistency with the NCCLS document C34 A-2. The most common cause of insufficient samples is the use of inappropriate collection devices (see CHM.29850).

COMMENTARY:

N/A

REFERENCE: Cystic Fibrosis Foundation Center Accreditation Guidelines. Bethesda, MD, 2004.

CHM.30200 **Phase II** **N/A YES NO**

Are the sweat samples labeled with appropriate patient identification?

NOTE: The label must be attached before determining the initial weight.

COMMENTARY:

N/A

CHM.30300

Phase II

N/A YES NO

Does the protocol describe the recognition of, and appropriate treatment for, patient skin reactions (allergic or burns) to pilocarpine and/or other reagents used in iontophoresis?

NOTE: Rarely, some patients may develop an area of, urticaria (hives) or small localized burns. In such cases, the procedure must be discontinued immediately and appropriate medical attention obtained. Sweat must not be collected over areas of urticaria or burns.

COMMENTARY:

N/A

.....

Analytic Methods for Sweat Testing

.....

CHM.30400

Phase II

N/A YES NO

For sweat testing, is the analytical method validated by the laboratory prior to patient testing using specimens equivalent to the volume and concentration of patient sweat samples?

NOTE: Validation procedures must include studies of accuracy, precision, and upper/lower limits of the analytic measurement range. The laboratory should be aware that some instruments designed for serum or urine electrolyte determination may lack the sensitivity required for sweat testing.

COMMENTARY:

N/A

REFERENCES: 1) Pillion DJ, Meczan E. Chloride measurement by microelectrode in cystic fibrosis and normal sweat. *Miner Electrolyte Metab.* 1987;13:196-200; 2) Barnes GL, *et al.* Sweat testing by capillary collection and osmometry: suitability of the Wescor macroduct system for screening suspected cystic fibrosis patients. *Aust Paediatr J.* 1988;24:191-193; 3) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Clinical laboratory improvement amendments of 1988; final rule. *Fed Register.* 2003(Jan 24):3707 [42CFR493.1255]; 4) NCCLS. Sweat testing: sample collection and quantitative analysis; approved guideline C34-A2. Wayne, PA: NCCLS, 2000; 5) Department of Health and Human Services, Centers for Medicare and Medicaid Services Center for Disease Control and Prevention. Medicare, Medicaid and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications; final rule. *Fed Register.* 2003 (Jan 24): Vol. 68, No. 16 [42CFR493].

patient, based on several variables. The laboratory must work cooperatively with the clinician to ensure that all necessary information is obtained.

CHM.31100**Phase II****N/A YES NO****Do prenatal screening requisitions solicit date of last menstrual period (LMP) or estimated gestational age by ultrasound dating?**

NOTE: Date of last menstrual period (LMP) or estimated gestational age by ultrasound dating must be included as part of the test requesting process. During the second trimester of pregnancy, MSAFP concentrations increase by about 15% per week of gestation, MSuE3 concentrations increase by about 25% per week, and hCG decreases from 15 to 18 weeks by about 15% and remains relatively constant thereafter. The optimum time for neural tube defect detection using MSAFP measurements is between 16-18 weeks gestation. Screening for fetal trisomies is acceptable from 15 to 21 weeks of gestation.

COMMENTARY:

N/A

REFERENCES: 1) Maternal serum-alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. Report of U.K. collaborative study on alpha-fetoprotein in relation to neural-tube defects. *Lancet*. 1977;i:1323-1332; 2) Wald NJ, *et al*. Maternal serum screening for down's syndrome in early pregnancy. *Brit Med J*. 1988;297:883-887; 3) Bock JL. Current issues in maternal serum alpha-fetoprotein screening. *Am J Clin Pathol*. 1992;97:541-554.

CHM.31200**Phase II****N/A YES NO****Do prenatal screening requisitions solicit maternal birth date?**

NOTE: Maternal birth date must be included as part of the test requesting process. Maternal age is not necessary when screening for neural tube defects, but is needed to calculate the patient-specific risk for Down syndrome. The patient-specific risk, not the analyte level, is used as the screening variable to identify pregnancies at high-risk for Down syndrome.

COMMENTARY:

N/A

REFERENCES: 1) Cuckle HS, *et al*. Estimating a woman's risk of having a pregnancy associated with down's syndrome using her age and serum alpha-fetoprotein level. *Brit J Obstet Gynecol*. 1987;94:387-402; 2) Wald NJ, *et al*. Maternal serum screening for down's syndrome in early pregnancy. *Brit Med J*. 1988;297:883-887.

CHM.31300**Phase II****N/A YES NO****Do prenatal screening requisitions solicit patient race?**

NOTE: Patient race must be included as part of the test requesting process. Black women have 10-15% higher MSAFP levels than caucasian women at the same gestational age, while MSuE3 levels are similar in the two racial groups. Data are conflicting for hCG, but the consensus estimate is that values are approximately 10% higher in black women as compared to caucasian women. Depending upon the racial distribution of the patient population, the laboratory should either have separate MSAFP medians for blacks and caucasians, or apply an appropriate correction factor for the non-numerically dominant race. Black women also have a lower birth prevalence of neural tube defects, and some screening programs raise the MoM cut-off to take this difference into account (after adjusting the AFP MoM value). MSuE3 levels should not be adjusted. Adjustment of hCG levels is not universally accepted at this time, but an emerging consensus indicates that adjustment is warranted (use of race-specific medians is also acceptable).

Current data indicate that statistically significant differences in median values exist for other races and ethnic groups (e.g., Hispanic, Asian, Indian). Most differences tend to be small, and do not materially affect the risk calculations for Down syndrome and neural tube defects. However, laboratories that screen large numbers of women may consider using median values specific to ethnic or racial groups if in their screening population significant differences are identified.

COMMENTARY:

N/A

REFERENCES: 1) Crandall BF, *et al.* Alpha-fetoprotein concentrations in maternal serum: relation to race and body weight. *Clin Chem.* 1983;29:531-533; 2) Greenberg F, *et al.* Estimates of birth prevalence rates of spina bifida in the United States from computer-generated maps. *Am J Obstet Gynecol.* 1983;145:570-573; 3) Bock JL. Current issues in maternal serum alpha-fetoprotein screening. *Am J Clin Pathol.* 1992;97:541-554; 4) Kulch P, *et al.* Racial differences in maternal serum human chorionic gonadotrophin and unconjugated oestriol levels. *Prenat Diag.* 1993;13:191-195; 5) O'Brien JE, Dvorin E, Drugan A, Johnson MP, Yaron TY, Evans MI. Race-ethnicity -specific variation in multiple-marker biochemical screening: alpha-fetoprotein, hCG, and estriol. *Obstet Gynecol* 1997 89(3):355-8; 6) Benn PA, Clive JM, Collins R. Medians for second-trimester maternal serum alpha-fetoprotein human chorionic gonadotrophin, and unconjugated estriol; differences between races or ethnic groups. *Clin Chem* 1997 43(2):333-7.

CHM.31400**Phase II****N/A YES NO****Do prenatal screening requisitions solicit maternal weight?**

NOTE: Maternal weight must be included as part of the test requesting process. The average concentration of all of the analytes used for screening decreases with increasing maternal weight.

Heavier women have lower analyte values, and lighter women have higher levels. This is presumably due to a greater maternal blood volume in the former group. The influence of weight adjustment on neural tube defects screening is small, but worthwhile. Maternal weight adjustment of AFP, uE3, and hCG does not have a significant impact on overall detection and false positive rates for Down syndrome screening. This is because the decrease in AFP and uE3 MoM values observed with increasing weight is associated with increased risk, but decreased hCG values are associated with decreased risk. These effects cancel for most women, and the risk calculated before and after weight correction is small. However, for some women the effect is more pronounced, and weight adjustment is therefore recommended.

COMMENTARY:

N/A

REFERENCES: 1) Johnson AM, *et al.* The effect of adjusting maternal serum alpha-fetoprotein levels for maternal weight in pregnancies with open spina bifida: a United States collaborative study. *Am J Obstet Gynecol.* 1990;163:9-11; 2) Bock JL. Current issues in maternal serum alpha-fetoprotein screening. *Am J Clin Pathol.* 1992;97:541-554; 3) Neveux LM, *et al.* Refinements in managing maternal weight adjustment for interpreting prenatal screening results. *Prenat Diag.* 1996;16:1115-1119.

CHM.31500**Phase II****N/A YES NO****Do prenatal screening requisitions solicit history of insulin-dependent diabetes mellitus?**

NOTE: History of insulin-dependent diabetes mellitus (IDDM) must be included as part of the test requesting process. Pregnant women who require insulin before pregnancy have 20% lower MSAFP levels than non-diabetics of the same gestational age, but have a higher birth prevalence of neural tube defects. If medians derived from non-diabetic women are used to screen women with IDDM, the percentage of women with values above the laboratory's MoM screening cut-off will be inappropriately low, resulting in a lower detection rate. Conversely, if medians from non-diabetic women are used for screening pregnancies from women with IDDM for Down syndrome, the AFP MoM values calculated using non-diabetic medians will be inappropriately low, resulting in an increased number of patients in the screen positive group. Available evidence indicates that uE3 and hCG are not significantly different in IDDM, and adjustment is not recommended for these analytes.

COMMENTARY:

N/A

REFERENCES: 1) Wald NJ, *et al.* Maternal serum alpha-fetoprotein and diabetes mellitus. *Br J Obstet Gynecol.* 1979;86:101-105; 2) Kucera J. Rate and type of congenital anomalies among offspring of diabetic women. *J Reprod Med.* 1979;7:61-70; 3) Greene MF, *et al.* Maternal serum alpha-fetoprotein levels in diabetic pregnancies. *Lancet.* 1988;ii:345-346; 4) Wald NJ, *et al.* Maternal serum unconjugated oestriol, human chorionic gonadotrophin, and alpha-fetoprotein levels in pregnancies

with insulin-dependent diabetes: implications for Down's syndrome screening. *Brit J Obstet Gynaecol.* 1992;99:51-53.

CHM.31600**Phase II****N/A YES NO**

Do prenatal screening requisitions solicit clinical evidence of multiple gestations (twins, etc.)?

NOTE: Clinical evidence of multiple gestations (twins, etc.) must be included as part of the test requesting process. Women with ultrasonographically confirmed twin pregnancies have, on average, twice the level of MSAFP than women with singleton pregnancies at the same gestational age. Most laboratories use a screening cut-off level for twin pregnancies between 3.5-5.0 MoM, or divide the MoM by 2 and use the same cut-off level as for singleton pregnancies. However, screening for neural tube defects in twin pregnancies is less efficient than singleton pregnancies. Approximately 50% of twin pregnancies with an open neural tube defect and 5% of unaffected twin pregnancies have a MoM of 4.5 or greater. Insufficient data are available to interpret MSAFP measurements in pregnancies with three or more fetuses. hCG levels are also approximately twice as high in twin pregnancies, while uE3 levels in twin pregnancies are approximately 1.7 times as high as in singleton pregnancies. If twin pregnancies are to be screened for Down syndrome, laboratories need to calculate risks using a method specifically designed for this application.

COMMENTARY:

N/A

REFERENCES: 1) Cuckle HS, *et al.* Maternal serum alpha-fetoprotein screening for open neural tube defects in twin pregnancies. *Prenat Diagn.* 1990;10:71-77; 2) Bock JL. Current issues in maternal serum alpha-fetoprotein screening. *Am J Clin Pathol.* 1992;97:541-554; 3) Wald NJ, *et al.* Maternal serum unconjugated oestriol and human chorionic levels in twin pregnancies: implications for screening for Down's syndrome. *Brit J Obstet Gynaecol.* 1991;98:905-908.

CHM.31700**Phase I****N/A YES NO**

Do the test requisitions ask if this is the initial screening sample or a repeat test for this pregnancy?

NOTE: The interpretation of a repeat maternal serum sample may be different from the interpretation of an initial serum specimen. In neural tube defect screening using AFP, a repeat sample can be interpreted as if it were an initial sample if fixed MoM cut-offs are used to identify high-risk women. If patient-specific risks are calculated for a repeat test result, one should combine the results of both the initial and repeat sample, using published algorithms. Repeat testing is not recommended for Down syndrome screening unless a sample is drawn too early for reliable interpretation. If a test on a second sample is performed, it is essential that the revised risk be calculated using the results from both samples. A method has been published for these calculations.

COMMENTARY:

N/A

REFERENCES: 1) Estimating an individual's risk of having a fetus with open spina bifida and the value of repeat alpha-fetoprotein testing. Fourth report of the U.K. collaborative study on alpha-fetoprotein in relation to neural tube defects. *J Epidemiol Commun Health*. 1982;36:87-95; 2) Cuckle HS, *et al*. Repeat maternal serum testing in multiple marker down's syndrome screening programmes. *Prenat Diagn*. 1994;14:603-607.

CHM.31800**Phase II****N/A YES NO**

Is there documentation that the laboratory has established its own median values or verified that the manufacturer's package insert or other source of medians is appropriate for the population being screened?

NOTE: Systematic biases in maternal serum assay values of up to 30% can occur when kits from different manufacturers are used. In addition, between-laboratory differences in equipment, reagents, and technique may introduce bias in assay results even when the same kit is used. These differences can be minimized by reporting results in multiples of the normal median (assuming that the medians are calculated using values measured on the population to be tested using the kit designated for screening). Package insert medians may be outdated or inappropriate and should only be used as a general guide to expected medians. Incorrect reference data may lead to inappropriate recommendations in the laboratory report.

COMMENTARY:

N/A

REFERENCES: 1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda, Maryland. The quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural-tube defects. *Clin Chim Acta*. 1980;105:9-24; 2) Knight GJ, *et al*. Assessing reliability of AFP test kits. *Contemp Obstet Gynecol*. 1987 (Technology issue);30:37-52; 3) NCCLS. Assessing the quality of systems for alpha-fetoprotein (AFP) assays used in prenatal screening and diagnosis of open neural tube defects; approved guideline I/LA17-A. Wayne, PA: NCCLS, 1997; 4) Knight GJ. Quality assessment of a prenatal screening program. *Early Human Development*. 1996;47(Supp):S49-S53.

CHM.31900**Phase II****N/A YES NO**

Are medians recalculated or reverified at least annually?

NOTE: This is a valuable quality control mechanism to ensure validity of reported MoMs.

COMMENTARY:

N/A

REFERENCES: 1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda, Maryland. The quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural-tube defects. *Clin Chim Acta*. 1980;105:9-24; 2) Bock JL. Current issues in maternal serum alpha-fetoprotein screening. *Am J Clin Pathol*. 1992;97:541-554.

CHM.32000**Phase II****N/A YES NO**

Are the percentages of women with screen-positive test results for both neural tube defects and Down syndrome calculated and reviewed at least quarterly?

NOTE: Data from large studies provide guidelines for the percentage of pregnancies that will fall above specified maternal serum AFP MoM levels (NTD screening) or with risks greater than specified risk cut-off levels (Down syndrome screening). Regular comparison of a laboratory's screen-positive rates with expected rates serves as a continuing measure of assay quality, appropriateness of medians, and accuracy of gestational dating.

COMMENTARY:

N/A

REFERENCES: 1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda Maryland. The quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural-tube defects. *Clin Chim Acta*. 1980;105:9-24; 2) Knight GJ, Palomaki GE. Epidemiologic monitoring and quality control of prenatal screening. *Proc UK NEQAS Meeting*. 1994;1:120-126.

CHM.32100**Phase I****N/A YES NO**

If the laboratory adds dimeric inhibin A (DIA) (or another marker) to its screening panel, has it followed the same requirements outlined for established markers?

NOTE: Some screening laboratories are currently adding a fourth marker, dimeric inhibin A, to the triple test. If so, the laboratory should be able to document that it adheres to the checklist items outlined for established markers in the Prenatal Screening section. These include establishing median values appropriate for the population being screened, and adjusting where appropriate for variables that have been shown to influence analyte values, such as maternal weight, maternal race, insulin dependent diabetes, and twin pregnancy. Laboratories should also verify that the risks calculated using the additional marker is valid.

NOTE: Reports must include data essential to the interpretation of the test results to enable both the laboratory and physician to ensure that the interpretations on the report are based on correct information.

COMMENTARY:

N/A

CHM.32400

Phase II

N/A YES NO

Are test results reported as multiples of the population median (MoM)?

NOTE: Reporting of results in terms of multiple of the population median (MoM) simplifies interpretation at various gestational ages, reduces possible systematic between-laboratory and between-kit bias in assay results, as well as facilitating comparison between laboratories. Laboratories can also compare their experiences with large-scale published studies more readily by using MoM as the reportable interpretive unit. The MoM is calculated as the measured analyte value divided by the median value for the appropriate gestational age. The MoM is also adjusted for those clinical variables known to influence the concentration of each analyte, generally by dividing by a factor specific for each variable.

COMMENTARY:

N/A

REFERENCES: 1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda Maryland. The quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural-tube defects. *Clin Chim Acta*. 1980;105:9-24; 2) NCCLS. Assessing the quality of systems for alpha-fetoprotein (AFP) assays used in the prenatal screening and diagnosis of open neural tube defects; approved guideline I/LA17-A. Wayne, PA: NCCLS, 1997.

CHM.32500

Phase I

N/A YES NO

Does the report classify a pregnancy as screen-positive or screen-negative for open neural tube defects, based on the MSAFP test results?

NOTE: Cut-off levels based on maternal serum AFP MoM values or risk have been established by large screening programs. Use of these cut-off values in the laboratory report can assist the physician in making clinical decisions about pregnancy management.

COMMENTARY:

COMMENTARY:

N/A

REFERENCES: 1) Amniotic-fluid alpha-fetoprotein measurement in antenatal diagnosis of anencephaly and open spina bifida in early pregnancy. Second report of the U.K. collaborative study on alpha-fetoprotein in relation to neural tube defects. *Lancet*. 1979;ii:651; 2) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda Maryland: the quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural-tube defects. *Clin Chim Acta*. 1980;105:9-24; 3) Knight GJ. Maternal serum alpha-fetoprotein screening. In: techniques in diagnostic human biochemical genetics. New York, NY: Wiley-Liss, 1991:503; 4) NCCLS. Assessing the quality of systems for alpha-fetoprotein (AFP) assays used in prenatal screening and diagnosis of open neural tube defects; approved guideline I/LA17-A. Wayne, PA: NCCLS, 1997.

CHM.32800 Phase II**N/A YES NO****Are AFAP medians recalculated or reverified at least annually?**

COMMENTARY:

N/A

CHM.32900 Phase II**N/A YES NO****Are AFAP results reported in multiples of the median (MoM)?**

NOTE: Reporting of AFAP results in terms of multiples of the median (MoM) simplifies interpretation at various gestational weeks, reduces the systematic between-laboratory and between-kit bias in results, and facilitates comparison of results between laboratories. Laboratories may compare their experiences with large-scale published studies much more readily when using MoM as the interpretive unit for AFP measurements.

COMMENTARY:

N/A

REFERENCES: 1) Report of a workshop sponsored by the National Institute of Child Health and Human Development (NICHD), Bethesda, Maryland: the quality control of alpha-fetoprotein reagents and assay for the antenatal screening and diagnosis of open neural-tube defects. *Clin Chim Acta*. 1980;105:9-24; 2) Wald NJ, *et al*. Amniotic fluid acetylcholinesterase measurement in the prenatal diagnosis of open neural tube defects. *Prenat Diagn*. 1989;9:813-829; 3) NCCLS. Assessing the

N/A

REFERENCES: 1) Haddow JE, *et al.* Acetylcholinesterase and fetal malformations: modified qualitative technique for diagnosis of neural tube defects. *Clin Chem.* 1981;27:61-63; 2) Report of the collaborative acetylcholinesterase study. Amniotic fluid acetylcholinesterase electrophoresis as a secondary test in the diagnosis of anencephaly and open spina bifida in early pregnancy. *Lancet.* 1981;ii:321-324; 3) Wald N, *et al.* Amniotic fluid acetylcholinesterase measurement in the prenatal diagnosis of open neural tube defects. *Prenat Diagn.* 1989;9:813-829.

CHM.33300

Phase II

N/A YES NO

If acetylcholinesterase is run in-house, are both positive and negative controls included with each analytic run?

COMMENTARY:

N/A

REFERENCES: 1) Haddow JE, *et al.* Acetylcholinesterase and fetal malformations: modified qualitative technique for diagnosis of neural tube defects. *Clin Chem.* 1981;27:61-63; 2) Report of the collaborative acetylcholinesterase study. Amniotic fluid acetylcholinesterase electrophoresis as a secondary test in the diagnosis of anencephaly and open spina bifida in early pregnancy. *Lancet.* 1981;ii:321-324; 3) Wald NJ, *et al.* Amniotic fluid acetylcholinesterase measurement in the prenatal diagnosis of open neural tube defects. *Prenat Diagn.* 1989;9:813-829.

CHM.33400

Phase II

N/A YES NO

If acetylcholinesterase is run in-house, are acetylcholinesterase-positive results confirmed by addition of a specific inhibitor?

NOTE: Positive acetylcholinesterase results must be confirmed by the addition of a specific inhibitor of acetylcholinesterase, such as BW284C51.

COMMENTARY:

N/A

REFERENCE: Barlow RD, *et al.* A single method for amniotic fluid gel-acetylcholinesterase determination, suitable for routine use in antenatal diagnosis of open neural-tube defects. *Clin Chim Acta.* 1982;119:137-142.

R, *et al*, eds. Hematology: basic principles and practice. New York, NY: Churchill-Livingstone, 1991:1815-1827; 12) Mallory PA, *et al*. Comparison of isoelectric focusing and cellulose acetate electrophoresis for hemoglobin separation. *Clin Lab Sci*. 1994;7:348-35; 13) Awalt E, *et al*. Tandem mass spectrometry (MS) – A screening tool for hemoglobinopathies. *Clin Chem*. 2001;47(suppl):A165; 14) Bradley CA, Kelly A. Comparison of high performance liquid chromatography with electrophoresis for measurement of hemoglobins A, A2, S, F, and C. *Clin Chem*. 2001;47(suppl):A172; 15) Bradley CA, Kelly A. Calibration verification of hemoglobins A, A2, S, and F with an automated chromatography system. *Clin Chem*. 2001;47(suppl):A17315; 16) Hoyer JD, *et al*. Flow cytometric measurement of hemoglobin F in RBCs: diagnostic usefulness in the distinction of hereditary persistence of fetal hemoglobin (HPFH) and hemoglobin S-HPFH from other conditions with elevated levels of hemoglobin F. *Am J Clin Pathol*. 2002;117:857-863.

CHM.33732

Phase II

N/A YES NO

Are all samples with hemoglobin variants migrating in "non-A, non-S" positions on alkaline electrophoresis, isoelectric focusing, or HPLC further defined with electrophoresis at acid pH or other acceptable methods where clinically and technically appropriate?

NOTE: Electrophoresis at acid pH is useful to further characterize hemoglobin variants migrating in the Hb A2 position, if all variants are not clearly separated by the primary method. This method will differentiate the three major hemoglobins that migrate in this position, namely Hb C, Hb E, and Hb O-Arab, as well as give information on rare variants such as Hb C-Harlem. However, for hemoglobin variants that migrate in other "non-A, non-S" positions, such as fast hemoglobin variants, electrophoresis at acid pH is generally not informative. Further workup of such variants, including referral to a reference laboratory, is dependent upon the patient's overall clinical situation, such as findings of erythrocytosis or a hemolytic anemia.

COMMENTARY:

N/A

REFERENCES: 1) Glacteros F, *et al*. Cord blood screening for hemoglobin abnormalities by thin layer isoelectric focusing. *Blood*. 1980;56:1068; 2) Beuzard Y, *et al*. Isoelectric focusing of human hemoglobins, In Hanash, Brewer, eds. Advances in hemoglobin analysis. New York, NY: Alan R. Liss, 1981:177-195; 3) Black J. Isoelectric focusing in agarose gel for detection and identification of hemoglobin variants. *Hemoglobin*. 1984;8:117; 4) Bunn HF, Forget BG. Hemoglobin: molecular, genetic and clinical aspects. Philadelphia, PA: WB Saunders, 1986; 5) Fishleder AJ, Hoffman GC. A practical approach to the detection of hemoglobinopathies: part I. The introduction and thalassemia syndromes. *Lab Med*. 1987;18:368-372; 6) Fishleder AJ, Hoffman GC. A practical approach to the detection of hemoglobinopathies: part II. The sickle cell disorders. *Lab Med*. 1987;18:441-443; 7) Fishleder AJ, Hoffman GC. A practical approach to the detection of hemoglobinopathies: part III. Nonsickling disorders and cord blood screening. *Lab Med*. 1987;18:513-518; 8) Adams JG III, Steinberg MH. Analysis of hemoglobins, In Hoffman R, *et al*, eds. Hematology: basic principles and practice. New York, NY: Churchill-Livingstone, 1991:1815-1827; 9) Mallory PA, *et al*. Comparison of isoelectric focusing and cellulose acetate electrophoresis for hemoglobin separation. *Clin Lab Sci*.

1994;7:348-352; 10) Ou C-N, Rognerud CL. Rapid analysis of hemoglobin variants by cation exchange HPLC. *Clin Chem.* 1993;39:820-824; 11) Awalt E, *et al.* Tandem mass spectrometry (MS) – A screening tool for hemoglobinopathies. *Clin Chem.* 2001;47(suppl):A165; 12) Bradley CA, Kelly A. Comparison of high performance liquid chromatography with electrophoresis for measurement of hemoglobins A, A2, S, F, and C. *Clin Chem.* 2001;47(suppl):A172; 13) Bradley CA, Kelly A. Calibration verification of hemoglobins A, A2, S, and F with an automated chromatography system. *Clin Chem.* 2001;47(suppl):A173; 14) Hoyer JD, *et al.* Flow cytometric measurement of hemoglobin F in RBCs: diagnostic usefulness in the distinction of hereditary persistence of fetal hemoglobin (HPFH) and hemoglobin S-HPFH from other conditions with elevated levels of hemoglobin F. *Am J Clin Pathol.* 2002;117:857-863.

CHM.33764

Phase II

N/A YES NO

Are all samples that appear to have Hb S as the predominant band by the primary screening (by whatever method) and that are confirmed as sickling by appropriate methods further examined to ascertain whether the "Hb S" band or peak contains solely Hb S or both Hb S and Hb D, Hb G or other variant hemoglobins?

NOTE: When the predominant hemoglobin component appears to be Hb S, it is necessary to determine whether this represents homozygous Hb S or a heterozygote for Hb S and another variant such as Hb D, Hb G, Hb Lepore, or other hemoglobin variant(s). Given the clinical implications of homozygous Hb S (or Hb S/β-zero thalassemia) it is imperative to exclude other hemoglobin variants, however rare. Referral of these specimens to a reference laboratory for further workup is acceptable.

COMMENTARY:

N/A

REFERENCES: 1) Black J. Isoelectric focusing in agarose gel for detection and identification of hemoglobin variants. *Hemoglobin.* 1984;8:117; 2) Bunn HF, Forget BG. Hemoglobin: molecular, genetic and clinical aspects. Philadelphia, PA: WB Saunders, 1986; 3) Fishleder AJ, Hoffman GC. A practical approach to the detection of hemoglobinopathies: part I. The introduction and thalassemia syndromes. *Lab Med.* 1987;18:368-372; 4) Fishleder AJ, Hoffman GC. A practical approach to the detection of hemoglobinopathies: part II. The sickle cell disorders. *Lab Med.* 1987;18:441-443; 5) Fishleder AJ, Hoffman GC. A practical approach to the detection of hemoglobinopathies: part III. Nonsickling disorders and cord blood screening. *Lab Med.* 1987;18:513-518; 6) Adams JG III, Steinberg MH. Analysis of hemoglobins, In Hoffman R, *et al.*, eds. Hematology: basic principles and practice. New York, NY: Churchill-Livingstone, 1991:1815-1827; 7) Mallory PA, *et al.* Comparison of isoelectric focusing and cellulose acetate electrophoresis for hemoglobin separation. *Clin Lab Sci.* 1994;7:348-352.

1995;2:195-199; 7) O'Mara K, Sullivan B. A simple bedside test to identify ulnar collateral flow. *Ann Intern Med.* 1995;123:637; 8) Starnes SL, *et al.* Noninvasive evaluation of hand circulation before radial artery harvest for coronary artery bypass grafting. *J Thorac Cardiovasc Surg.* 1999;117:261-266; 9) Cable DG, *et al.* The Allen test. *Ann Thorac Surg.* 1999;67:876-877.

CHM.34000**Phase II****N/A YES NO**

Is there a system to prevent ambient air contamination of blood gas samples before analysis?

COMMENTARY:

N/A

REFERENCES: 1) Ishikawa S, *et al.* The effects of air bubbles and time delay on blood gas analysis. *Ann Allergy.* 1974;33:72-77; 2) Mueller RG, *et al.* Bubbles in samples for blood gas determinations. *Am J Clin Pathol.* 1976;65:242-249; 3) Madieto G, *et al.* Air bubbles and temperature effect on blood gas analysis. *J Clin Pathol.* 1980;33:864-867; 4) Biswas CK, *et al.* Blood gas analysis: effect of air bubbles in syringe and delay in estimation. *Brit Med J.* 1982;284:923-927; 5) McKane MH, *et al.* Sending blood gas specimens through pressurized transport tube systems exaggerates the error in oxygen tension measurements created by the presence of air bubbles. *Anesth Analg.* 1995;81:179-182; 6) Astles JR, *et al.* Pneumatic transport exacerbates interference of room air contamination in blood gas samples. *Arch Pathol Lab Med.* 1996;120:642-647.

BLOOD GAS INSTRUMENTS

If the institution has blood gas testing sites that are medically and/or administratively separate from the main laboratory, and the blood gas testing medical director is different from the central laboratory medical director, then a separate Chemistry and Toxicology Checklist must be completed. If blood gas analyses are performed in a central laboratory with other chemistry assays, and/or testing occurs physically separate from the main laboratory, but the medical director is the same as the main laboratory, then complete this section.

CHM.34100**Phase II****N/A YES NO**

Are there documented procedures for operation, calibration, and function checks of all blood gas instruments?

COMMENTARY:

N/A

CHM.34500

Phase II

N/A YES NO

Do the control materials for pH, pCO2 and pO2 represent both high and low values on each day of patient testing?

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24) [42CFR493.1267(b)]; 2) NCCLS. Statistical quality control for quantitative measurements: principles and definitions - second edition; approved guideline C24-A2. Wayne, PA: NCCLS, 1998; 3) Ng VL, *et al.* The rise and fall of i-STAT point-of-care blood gas testing in an acute care hospital. *Am J Clin Pathol*. 2000;114:128-138.

CHM.34600

Phase II

N/A YES NO

Is at least one sample of control material for pH, pCO2 and pO2 included each time patient specimens are tested, except for automated instruments that internally calibrate at least once every 30 minutes of use?

COMMENTARY:

N/A

REFERENCES: 1) Department of Health and Human Services, Centers for Medicare and Medicaid Services. Medicare, Medicaid and CLIA programs; CLIA fee collection; correction and final rule. *Fed Register*. 2003(Jan 24): 3709 [42CFR493.1267(c)]; 2) NCCLS. Statistical quality control for quantitative measurements: principles and definitions - second edition; approved guideline C24-A2. Wayne, PA: NCCLS, 1998.

#####

LEGAL TESTING

#####

Some laboratories may choose to perform certain tests exclusively for legal purposes (e.g., alcohol for traffic law enforcement, criminal justice and medical examiner systems). In this case, the performance of legal testing must meet forensic, not clinical laboratory, standards. These forensic standards include the requirements for chain-of-custody protocols for specimens and aliquots, specimen seals,

guideline T/DM6-A. Wayne, PA: NCCLS, 1997; 5) Sylvester PA, *et al.* Unacceptably high site variability in postmortem blood alcohol analysis. *J Clin Pathol.* 1998;51:250-252; 6) Williams RH, Leikin JB. Medicolegal issues and specimen collection for ethanol testing. *Lab Med.* 1999;30:530-537.

CHM.36900**Phase I****N/A YES NO**

Has the laboratory evaluated the effectiveness of its specimen collection containers in maintaining analyte stability?

NOTE: The laboratory should evaluate the effectiveness of its specimen collection containers in accurately maintaining analyte stability over time, as changes may occur that would alter the validity of reported measurements. For example, both metabolic consumption of alcohol and production of alcohol by microorganisms must be considered.

COMMENTARY:

N/A

REFERENCES: 1) Brown GA, *et al.* The stability of ethanol in stored blood. Part 1. Important variables and interpretation of results. *Analyt Chim Acta.* 1973;66:271-283; 2) Kaye S. The collection and handling of the blood alcohol specimen. *Am J Clin Pathol.* 1980;74:743-746; 3) Winek CL, Paul LJ. Effect of short-term storage conditions on alcohol concentrations in blood from living human subjects. *Clin Chem.* 1983;29:1959-1960; 4) Dubowski KM, *et al.* The stability of ethanol in human whole blood controls: an inter-laboratory study. *J Analyt Toxicol.* 1997;21:486-491.

CHM.37000**Phase II****N/A YES NO**

If the laboratory tests for legal alcohols, has the method been evaluated for ethanol specificity?

NOTE: An alcohol (ethanol) specific methodology must be in use.

COMMENTARY:

N/A

REFERENCES: 1) Dubowski KM. Alcohol determination in the clinical laboratory. *Am J Clin Pathol.* 1980;74:747-750; 2) NCCLS. Blood alcohol testing in the clinical laboratory; approved guideline T/DM6-A. Wayne, PA: NCCLS, 1997; 3) Osterloh JD, *et al.* Discrepancies in osmolal gaps and calculated alcohol concentrations. *Arch Pathol Lab Med.* 1996;120:637-341; 4) Williams RH, Leikin JB. Assessment of ethanol intoxication and regulatory issues. *Lab Med.* 1999;30:587-594.

CHM.37100 **Phase II** **N/A YES NO**

Does the specimen receiving/accessioning procedure require documentation of type of specimen, verification of specimen identity, completeness of external chain-of-custody documents, and integrity (tamper-evident) of the transmittal or shipping container?

COMMENTARY:

N/A

CHM.37200 **Phase II** **N/A YES NO**

Does the laboratory properly complete appropriate sections of external chain-of-custody documents?

COMMENTARY:

N/A

CHM.37300 **Phase II** **N/A YES NO**

Is there a requirement for preparation of internal chain-of-custody documentation for specimens received?

COMMENTARY:

N/A

CHM.37400 **Phase II** **N/A YES NO**

Does the laboratory generate and properly complete internal chain-of-custody documents to account for the specimens and aliquots?

NOTE: The chain-of-custody procedure must account for all authorized individuals who handle the specimens/aliquots, or the storage location when not in the possession of an authorized individual. The reason for the transfer of custody should be recorded along with the date of the transfer.

COMMENTARY:

N/A

