



STATE OF NEW YORK DEPARTMENT OF HEALTH

Wadsworth Center The Governor Nelson A. Rockefeller Empire State Plaza
Antonia C. Novello, M.D., M.P.H., Dr. P.H.
Commissioner

P.O. Box 509 Albany, New York, 12201-0509
Dennis P. Whalen
Executive Deputy Commissioner

CLINICAL LABORATORY EVALUATION PROGRAM SUBMISSION GUIDELINES FOR TEST APPROVAL Trace Element Testing – Alternate Matrices

Subsection 58-1.10 of Part 58 of Title 10 (Health) of the Official Compilation of Codes, Rules and Regulations of the State of New York states that *all technical procedures employed in a laboratory shall be of proven reliability and generally accepted by leading authorities in the specialties of laboratory medicine and/or approved by the Department*. A laboratory shall perform only those assays that have been validated or verified at the site where the assay will be performed; must hold the appropriate permit category for the test; and must meet all other requirements related to personnel and proficiency testing.

The Clinical Laboratory Evaluation Program (CLEP) has written general submission guidelines that are available on the web site at [www.wadsworth.org/labcert/lep.html](http://www.wadsworth.org/labcert/clep/lep.html). The guidelines that follow are specific to validate the use of matrices other than whole blood, urine, serum or plasma for trace element testing. Periodically since 1986, we have surveyed the current thinking of leading authorities on the potential obstacles to validating alternate matrices such as hair, packed red cells, nails, and saliva. Although the medical community has not generally adopted these alternate matrices, we will consider the use of alternate matrices with the support of well-documented studies that address the following issues:

- Establishment of clinical validity. While peer-reviewed publications can be submitted in support of clinical validity, such studies cannot be used exclusively for this purpose. Published recommendations from appropriate government agencies (state or federal) may also be submitted to support the case for clinical validity. In-house clinical studies must include a significant number of samples from subjects that have been independently classified as with and without the clinical condition of interest.
- Pre-analytical variables: Contamination and interfering substances. This is especially noted for hair, which is subject to many contamination problems from hair treatments. Laboratory studies must demonstrate that the devices used to cut the hair do not introduce contamination.
- Analytical phase issues: matrix interferences; polyatomic/isobaric interferences (ICPMS) and/or background correction issues (AAS); matrix-based QC materials and/or matrix-based certified reference CRMs for periodic validation.

It is the responsibility of a laboratory proposing to offer this testing for patient care to validate its procedures completely with well-defined reference intervals. Such studies should be consistent with the CLSI document C28-A2. Should any laboratory design and conduct rigorous investigations to establish valid reference intervals for such analysis, the Department would consider those findings within the context of peer-reviewed literature and the opinions of leading scientific authorities. Please submit validation packages as outlined in these guidelines with completed Section I and Section II to identify where in the package each element can be retrieved.

Proprietary submissions:

Please note that materials submitted, including related data packages, cannot be returned to the laboratory. All materials are automatically treated in a manner that ensures confidentiality. In addition, if documents are marked "proprietary", laboratories will be given an opportunity to block information release if a request for the material is filed under the NYS Freedom of Information Law (FOIL), by presenting evidence that the materials contain trade secrets. Marking should minimally appear on the cover page of each unit of material. Documents not marked, or marked with terms such as "confidential" will not block release of the submission through a FOIL request.

SECTION I NOTIFICATION

Please submit the completed form (and attachments as necessary) by mail, email or on compact disc to:

Clinical Laboratory Evaluation Program, Wadsworth Center, New York State Department of Health, PO Box 509, Empire State Plaza, Albany, NY 12201-0509, Attn: Assay Validation Review. Email: CLEPCERT@health.state.ny.us

Laboratory: _____ **PFI:** _____ **Director:** _____

Address: _____ **Contact Person:** _____

Date: _____ **Phone:** _____ **Fax:** _____ **E-mail:** _____

- TEST INFORMATION AND CATEGORIZATION

Analyte: _____ **Specimen Type(s)** _____

Instrument Manufacturer: _____

Method/Procedure Principle: _____

- PERFORMANCE EVALUATION

- Test was validated through comparison to a reference assay. Describe the comparative method and/or identify the reference laboratory:

- Test was validated through correlation of test results to clinical status or condition of test subjects.

SECTION II ASSAY DESCRIPTION

Laboratories are required to submit the following documentation for in-house developed methods. Please organize enclosed items into attachments as indicated below. If an item is not included, indicate the reason. Include a complete SOPM and indicate the **page numbers** on which the items and/or attachments can be found.

- ATTACHMENT I: METHODS

- ___ Practitioner and patient educational materials that include a description of assay limitations
- ___ Clinical indications for testing, including, where appropriate, the prevalence and description of the medical condition.
- ___ Test subject preparation, specimen collection and handling, specimen rejection criteria, including a description of the mechanism to assure collection and transport requirements have been followed. See Trace Element Standard 2 and 7.
- ___ A description of the assay, assay principle and clinical validity.
- ___ Complete and detailed procedures for performing the assay, including algorithms and flowcharts as necessary and any safety considerations. See Trace Element Standards 8.
- ___ List of equipment / instrumentation essential to the assay.
- ___ Reagents: source, preparation, storage stability and handling.
- ___ Source and verification of standards / calibrators, quality control materials and the type, number, frequency and placement of the QC samples in an analytical run. See Trace Element Standards 5 and 6.
- ___ Calculation of results and interpretation. See Trace Element Standards 9.
- ___ Assay interferences and limitations.

- ATTACHMENT II: REQUISITION AND REPORTING

- ___ A sample requisition form.
- ___ Sample reports (in the laboratory's official report format) for all applicable findings including interpretive text, assay limitations (both diagnostic and technical limitations) and appropriate patient information

- ATTACHMENT III: REFERENCES

- ___ Copies of pertinent literature references that describe the scientific basis and clinical utility of the assay. References must not be based on animal models or epidemiological studies.

- ATTACHMENT IV: INITIAL VALIDATION PROTOCOL AND DATA

Describe the protocols used to validate the assay, including a description of the comparative method and the source and number of specimens. An overall narrative summary of the validation studies performed with results and conclusions must also be submitted. Data to demonstrate the following must be provided (please explain when data is not provided), using an appropriate number of samples across all representative specimen matrices and expected outcomes. Data should be summarized with clearly labeled tables, figures and photographs.

PRE-ANALYTIC PHASE

- ___ Analyte and matrix stability.
- ___ Specimen transport conditions.
- ___ Storage time and temperature.
- ___ For hair testing, at least 12 specimens in duplicate demonstrating the effects of any interferences (endogenous and exogenous).
- ___ Collection of hair samples describing the method used to cut the hair. Studies demonstrating that the method used for cutting does not contaminate the specimen.

ANALYTIC PHASE

- ___ Accuracy - studies must clearly describe the reference method and/or laboratory used for comparison. Recovery studies may also be performed.
- ___ Precision / reproducibility.
- ___ Reportable range / linearity
- ___ Method detection limit. See Trace Element Standard 1.

POST-ANALYTIC PHASE

- ___ Data reduction and interpretation.
- ___ Determination of the reference interval. The clinical status of the specimens used as the normal population must be known. It is unacceptable to use samples that have been received in the laboratory for other testing modules. Refer to CLSI C28-A2 for guidance
- ___ Clinical validity, data regarding the degree to which a result or variant predicts a disease or unhealthy state. must be established using specimens from patients with clinical status demonstrating absence of the condition or abnormality being assessed by the assay. Published literature, not including epidemiological studies or animal models, may be used. Complete copies of these references need to be included.

Where clinical investigations are necessary to determine clinical validity:

- ___ Describe the protocols used to determine the clinical status of test subjects.
- ___ Describe the procedure used to blind the clinical status of specimens during testing.
- ___ Describe the procedures used to resolve discrepant or equivocal test results.
- ___ Present data used for the determination of clinical sensitivity, specificity and/or predictive values.

SPECIMEN RUNS

- ___ Provide actual instrument printouts, worksheets, or charts from a representative run, including all standards and quality control materials. Include information to evaluate quality control.

- ATTACHMENT V: QUALITY ASSURANCE

- ___ Identify the critical steps in the test procedure and the quality control measures taken to control and monitor assay performance for consistent and reliable results.
- ___ Describe the mechanism that will be put in place to verify the accuracy and reliability of test results at least twice yearly for those elements not included in the NYS Proficiency Testing Program, as required in the NYS Quality Assurance Standards.