GLP 14

Good Laboratory Practice

for

Procedure for Method Validation

1 Introduction

This is the metrology laboratory policy and procedure for developing and validating test or calibration methods when no international or national procedures are available, when deviating from standardized methods, or when no standard procedures are available.

2 Purpose

The Metrology Laboratory follows this procedure to ensure that all laboratory methods selected, modified, or developed for tests and calibrations are appropriate for the intended use, properly documented, validated, accepted by laboratory management, and agreed upon by the client. Customers of the Laboratory expect a given service to provide acceptable measurement results when they request a test or calibration. The laboratory must evaluate each method to ensure that it has qualified and competent staff, suitable facilities, equipment, and standards with acceptable metrological traceability to perform the test or calibration.

3 Responsibility

3.1 The Laboratory Supervisor or Quality Manager ensures the following, in consultation with the laboratory staff as needed:

3.1.1 development of methods is a planned activity and assigned to qualified staff with appropriate resources;

3.1.2 for larger projects, plans are updated as progress is made and effectively communicated to all personnel; and

3.1.3 ensures the certificate for the test or calibration is compliant with standard requirements and customer needs.

3.2 The Technical Manager reviews the documented procedure, data, and analysis, and recommends final acceptance to the Laboratory Manager or Quality Manager based on the suitability of the procedure and acceptability of observed analysis of measurement results.

3.3 The Laboratory Supervisor or Quality Manager is responsible for final acceptance of new calibration methods, training staff on the new procedure, and for consistent implementation.

4 Operations

4.1 If the laboratory does not have an appropriate method for a calibration or test, or the test or calibration requires deviation to meet the needs of the customer, the Technical Manager is notified and this procedure is implemented.

4.2 When determining whether to proceed in developing new test or calibration method to meet the needs of a customer, the Laboratory Supervisor or Quality Manager and Technical Manager consider at least the following factors:

4.2.1 availability of alternative procedures (national or international standards);

4.2.2 resources of the laboratory and staffing (time, efficiency); and

4.2.3 likely future demand for the service.

4.3 The staff conducting the Contract Review for the calibration or test must obtain a clear specification of the customer requirements and the purpose of the test or calibration including any tolerances or maximum uncertainties that are required for the item/sample end usage (to ensure that the measurement results will be fit for purpose).

4.4 New methods must be developed prior to performing the tests or calibrations and contain the following information:

4.4.1 Appropriate identification (title);

4.4.2 Scope or range of test;

4.4.3 Description of the type of item to be tested or calibrated;

4.4.4 Parameters or quantities and ranges to be determined;

4.4.5 Apparatus and equipment, including technical performance requirements;

4.4.6 Reference standards and reference materials required;

4.4.7 Environmental conditions required, and any stabilization period needed;

4.4.8 Description of the procedure, including any special items as noted in this list:

4.4.8.1 Affixing of identification marks, handling, transporting, storing and preparation of items,

4.4.8.2 Checks to be made before the work is started,

4.4.8.3 Checks that the equipment is working properly and, where required, calibration and adjustment of the equipment before each use,

4.4.8.4 Method of recording the observations, data to be recorded, data reduction, method of analysis, and presentation of results, and

4.4.8.5 Safety measures to be observed;

4.4.9 Criteria and/or requirements for approval/rejection where applicable;

4.4.10 Data to be recorded and method of analysis and presentation; and

4.4.11 Uncertainty or the procedure for estimating uncertainty.

5 Method Validation

5.1 Non-standardized methods, which include all laboratory developed methods, standardized methods modified beyond their intended scope and amplifications and modifications of standardized methods, are validated by:

5.1.1 Examination to ensure completeness and compliance with requirements for essential components of metrological traceability; and

5.1.2 Analysis of objective evidence to ensure the requirements for a specific intended purpose are fulfilled prior to use.

5.2 Validation methods are to be as extensive as necessary to meet the needs of their intended application. Adequate measurement data is obtained to ensure statistical validity of the evaluated results. The accuracy and uncertainty of test or calibration results shall be assessed for the intended use, and shall be relevant to the client's needs.

5.3 Validation procedures and results are recorded, with a statement concerning the appropriateness of the new method as it pertains to the intended use.

5.4 Validation techniques include one or a combination of the following:

5.4.1 Calibration/verification and evaluation of bias and precision using calibrated working standards;

5.4.2 Comparison of results achieved with other standardized methods;

5.4.3 Method evaluation through variations of controlled parameters (e.g., one variable at a time) to determine robustness;

5.4.4 Inter-laboratory comparisons when practical;

5.4.5 Systematic assessment of factors influencing the results; and

5.4.6 Evaluation of the uncertainty of results based on scientific understanding of the theoretical principles associated with the method and practical experience.

5.5 When changes are made in the validated non-standardized procedures, the influence of such changes must be documented and, if appropriate, a new validation process carried out.

5.6 The following types of assessments, with data and statistical analysis are examples that may be used to assess the measurement results (See Appendix A form):

5.6.1 Inspection and technical assessment of the essential elements of metrological traceability to ensure presence and adequacy (technical review may include representatives from other laboratories, working groups, technical experts, and assessors):

5.6.1.1 Reference to the international system of units (SI);

5.6.1.2 Unbroken chain of calibrations to national and/or international standards;

5.6.1.3 Suitable and up to date calibration intervals for standards used in the procedure;

5.6.1.4 Documented procedure (reviewed to ensure completeness against the list of items in Section 4.d.);

5.6.1.5 Documented measurement uncertainty (as noted in Section 4.d.v.);

5.6.1.6 Demonstrated technical competence;

5.6.1.7 Adequate measurement assurance approach and supporting data.

5.6.2 Accuracy or Limits to Bias may use data obtained from internal testing and/or interlaboratory comparisons: t-test, normalized error (E_n), absolute or relative bias versus required tolerance limits;

5.6.3 Precision: standard deviation, normalized precision (P_n), F-test, comparison to required uncertainties (fit for purpose and meeting needs of the customer)

5.6.4 Repeatability: assessment of results over time and by different operators following the procedure as documented; and

5.6.5 Reproducibility: assessment of data from other laboratories following the procedure.

6 Records. (See Appendix A for summary of validation records to be supplemented with appropriate data, analysis, and evaluation records.)

6.1 Laboratory records shall be retained for all aspects of the procedure validation for as long as the procedure remains in valid use, including but not limited to:

6.1.1 Validation procedure (and version) that is used;

6.1.2 Any applicable specifications and/or tolerances;

6.1.3 Evaluation of performance characteristics and summaries;

6.1.4 Observed data and measurement results;

6.1.5 Approval for use by the customer; and

6.1.6 A statement that the method is valid and suitable for its intended use.

7 Implementation

7.1 A laboratory developed test or calibration method is validated, reviewed by the Technical Manager, reviewed by the Quality Manager, and approved by the Laboratory Supervisor.

7.2 The method is documented and formatted into a written Standard Operating Procedure (SOP) document and assigned an identification number. The new SOP will be added to the laboratory Master List.

7.3 Staff are trained and competency is confirmed.

7.4 All laboratory method validation documentation is kept on file in the laboratory and maintained according to the Quality Management System.

8 Acknowledgment and Validation

This publication was presented as part of a collection of draft Standard Administrative Procedures in 1996 and has been adopted by many weights and measures laboratories in some form since that time. The procedure has also been used in NIST seminars covering calibration procedure validation as a part of compliance with ISO/IEC 17025.

Appendix A

Evaluation Form for Method Validation Review

Procedure Evaluated: _____

Evaluation Conducted by: _____

Method Evaluation	Observations

Procedure is complete and contains:
☐ appropriate identification (title);
☐ scope or range of test;
☐ description of the type of item to be tested or calibrated;
☐ parameters or quantities and ranges to be determined;
☐ apparatus and equipment, including technical performance requirements;
☐ reference standards and reference materials required;
☐ environmental conditions required and any stabilization period needed;
☐ description of the procedure, including any special items as noted in this list:
  ☐ affixing of identification marks, handling, transporting, storing and preparation of items,
  ☐ checks to be made before the work is started,
  ☐ checks that the equipment is working properly and, where required, calibration and adjustment of the equipment before each use,
  ☐ the method of recording the observations, data to be recorded, data reduction, method of analysis, and presentation of results, and
  ☐ any safety measures to be observed;
☐ criteria and/or requirements for approval/rejection where applicable;
☐ data to be recorded and method of analysis and presentation; and
☐ the uncertainty or the procedure for estimating uncertainty.	

Essential Elements of Traceability are Defined (5.f, i) See GMP 13.	
Realization of SI Units. The primary national, international, or intrinsic standards must be primary standards for the realization of the International System of Units (SI);	
Unbroken chain of comparisons. A documented system of comparisons with each step having the essential elements of metrological traceability going back to a standard acceptable to the parties, usually a national or international standard; Are suitable standards identified in the procedure?	

Method Evaluation	Observations
Standard Calibrations & Intervals. Calibrations of standards (and equipment where appropriate) must be repeated at established (may be defined through measurement assurance) and appropriate intervals to preserve metrological traceability of the standard over time and use (see GLP 4, GMP 11); Are suitable calibration intervals defined for the standards used in this procedure?	
Documented Measurement Uncertainty. The measurement uncertainty for each step in the traceability chain must be calculated according to defined methods and must be stated so that an overall uncertainty for the whole chain may be calculated (see SOP 29); Is the uncertainty budget completely defined based on a comparison of similar procedures or technical reference documents (describe the procedures and/or references)	
Documented Measurement Procedure. Each step in the chain must be performed according to documented and generally acknowledged procedures (see GMP 12) and the results must be documented (i.e., in a calibration certificate, see SOP 1); Is the procedure complete according to all required elements? (4.d)	
Accredited Technical Competence. The laboratories or bodies performing one or more steps in the chain must supply evidence of technical competence (e.g., by maintaining appropriate training records, participating in interlaboratory comparisons, and by demonstrating that they are accredited by a recognized accreditation body); Have all staff been trained and have they demonstrated competency with the procedure? Have any other laboratories provided input or tried to duplicate the procedure? Was an interlaboratory comparison or proficiency test conducted? Describe the results.	
Measurement assurance. A proper measurement assurance program must be established to ensure the validity of the measurement process and the accuracy of standard used at the time of the measurement (see SOPs 9, 17, 20, 30). What type of measurement assurance is integrated into the procedure? Describe what the measurement assurance monitors (standards, process, both? How?)	
Additional Assessments	
Comparison of Results with Other Procedures. Describe what other procedures or standards were considered and why/why not chosen? Describe the results obtained and analysis conducted with multiple procedures.	
Evaluation of Accuracy and Bias. (5.f.ii) What are the limits to bias or error? How do you know the results are right? Describe the recently calibrated standard/set of standards that were used. Describe any standard reference materials that were used. How were the results assessed for Accuracy?	

Method Evaluation	Observations
Evaluation of Precision. How was data for repeatability obtained? Describe whether the precision assessment is short-term or long-term and if short-term, how do you know how the procedure will repeat over time? How do you know whether the precision is sufficiently small when incorporated into uncertainties? Describe the statistical assessments that were completed and document the analysis results.	
Evaluation of Repeatability. E.g., two different units were evaluated after a recent (enter dates) calibration by multiple metrologists; what kind of statistics were used and what were the results? (Consider repeatability with different staff, equipment, standards/nominal values, and not just short-term precision.)	
Evaluation of Reproducibility. Have any other laboratories provided input or tried to duplicate the procedure? Was an interlaboratory comparison or proficiency test conducted? Describe the results.	
3rd Party Assessment or Technical Reviews. Have any other technical experts reviewed the procedure and provided input? Describe their assessment and any recommended improvements or changes that were implemented because of the review.	

This procedure has found to be complete, fit for its intended use, technically validated, meets customer needs, and is approved for use.

Quality Manager Signature	Technical Manager Signature
Quality Manager Name (Printed)	Technical Manager Name (Printed)
Date	Date

Appendix B

Example Outline for a Standard Operating Procedure

(Title)

1 Scope and Measurand(s) of Calibrations

2 Description of the Item to be Calibrated

3 Measurement Parameters, Quantities, and Ranges to be Determined

4 Equipment, Including Technical Performance Requirements

5 Reference Standards and Reference Materials

6 Environmental Conditions and Stabilization Periods

7 Procedure Include any special items as noted in this list:

- 7.1 Affixing of identification marks, handling, transporting, storing and preparation of items;
- 7.2 Checks to be made before the work is started;
- 7.3 Checks that the equipment is working properly and, where required, calibration and adjustment of the equipment before each use;
- 7.4 Step by step process: the method of recording the observations, data to be recorded, data reduction, method of analysis, and presentation of results;
- 7.5 Any safety measures to be observed;
- 7.6 Criteria and/or requirements for approval/rejection where applicable;
- 7.7 Data to be recorded and method of analysis and presentation;

8 Calculations (See Possible Measurement Equations)

9 Measurement Assurance (possible Check Standards)

10 Uncertainties (include an Uncertainty Budget Table)

11 Calibration Certificate

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