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Standard Practice for Validation of the Performance of Multivariate Online, At-Line, and Laboratory Infrared Spectrophotometer Based Analyzer Systems[1]

This standard is issued under the fixed designation D6122; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

INTRODUCTION

Operation of a laboratory or process stream analyzer system typically involves four sequential activities. *(1)* **Analyzer Calibration**—When an analyzer is initially installed, or after major maintenance has been performed, diagnostic testing is performed to demonstrate that the analyzer meets the manufacturer's specifications and historical performance standards. These diagnostic tests may require that the analyzer be adjusted so as to provide predetermined output levels for certain reference materials. *(2a)* **Correlation, where analyzer and Primary Test Method (PTM) measure the same material**—Once the diagnostic testing is completed, process stream samples are analyzed using both the analyzer system and the corresponding PTM. A mathematical function is derived that relates the analyzer output to the PTM. The application of this mathematical function to an analyzer output produces a Predicted Primary Test Method Result (PPTMR) for the same material. *(2b)* **Correlation, where analyzer measures a material which is subjected to treatment before being measured by the PTM**—Once the diagnostic testing is completed, the process stream samples are analyzed by the analyzer system. The same samples are subjected to a consistent treatment, and the treated samples are analyzed by the PTM. A mathematical function is derived that related the analyzer output for the untreated sample to the Primary Test Method Result (PTMR) for the treated material. The application of the mathematical function to the analyzer output for the untreated material produces a PPTMR for the treated material. *(3)* **Probationary Validation**—Once the relationship between the analyzer output and PTMRs has been established, a probationary validation is performed using an independent but limited set of materials that were not part of the correlation activity. This probationary validation is intended to demonstrate that the PPTMRs agree with the PTMRs to within user-specified requirements for the analyzer system application. *(4)* **General and Continual Validation**—After an adequate number of PPTMRs and PTMRs have been accrued on materials that were not part of the correlation activity, a comprehensive statistical assessment is performed to demonstrate that the PPTMRs agree with the PTMRs to within user-specified requirements. Subsequent to a successful general validation, quality assurance control chart monitoring of the differences between PPTMR and PTMR is conducted during normal operation of the process analyzer system to demonstrate that the agreement between the PPTMRs and the PTMRs established during the General Validation is maintained. This practice deals with the third and fourth of these activities.

"Correlation where analyzer measures a material which is subjected to treatment before being measured by the PTM" as outlined in this practice is intended primarily to be applied to biofuels where the biofuel material is added at a terminal or other facility and not included in the process stream material sampled by the analyzer at the basestock manufacturing facility. The "treatment" shall be a constant percentage addition of the biofuels material to the basestock material.

1. Scope*

1.1 This practice covers requirements for the validation of measurements made by laboratory or process (online or at-line) near- or mid-infrared analyzers, or both, used in the calculation of physical, chemical, or quality parameters (that is, properties) of liquid petroleum products and fuels. The properties are calculated from spectroscopic data using multivariate modeling methods. The requirements include verification of adequate instrument performance, verification of the applicability of the calibration model to the spectrum of the sample under test, and

*A Summary of Changes section appears at the end of this standard

verification that the degree of agreement between the results calculated from the infrared measurements and the results produced by the PTM used for the development of the calibration model meets user-specified requirements. When there is adequate variation in property level, the statistical methodology of Practice D6708 is used to provide general validation of this equivalence over the complete operating range of the analyzer. For cases where there is inadequate property variation, methodology for level specific validation is used.

1.1.1 For some applications, the analyzer and PTM are applied to the same material. The application of the multivariate model to the analyzer output (spectrum) directly produces a PPTMR for the same material for which the spectrum was measured. The PPTMRs are compared to the PTMRs measured on the same materials to determine the degree of agreement.

1.1.2 For other applications, the material measured by the analyzer system is subjected to a consistent treatment prior to being analyzed by the PTM. The application of the multivariate model to the analyzer output (spectrum) produces a PPTMR for the treated material. The PPTMRs based on the analyzer outputs are compared to the PTMRs measured on the treated materials to determine the degree of agreement.

1.2 Performance Validation is conducted by calculating the precision and bias of the differences between results from the analyzer system (or subsystem) produced by application of the multivariate model, (such results are herein referred to as PPTMRs), versus the PTMRs for the same sample set. Results used in the calculation are for samples that are not used in the development of the multivariate model. The calculated precision and bias are statistically compared to user-specified requirements for the analyzer system application.

1.2.1 For analyzers used in product release or product quality certification applications, the precision and bias requirement for the degree of agreement are typically based on the site or published precision of the PTM.

NOTE 1—In most applications of this type, the PTM is the specification-cited test method.

1.2.2 This practice does not describe procedures for establishing precision and bias requirements for analyzer system applications. Such requirements must be based on the criticality of the results to the intended business application and on contractual and regulatory requirements. The user must establish precision and bias requirements prior to initiating the validation procedures described herein.

1.3 This practice does not cover procedures for establishing the calibration model (correlation) used by the analyzer. Calibration procedures are covered in Practices E1655 and references therein.

1.4 This practice is intended as a review for experienced persons. For novices, this practice will serve as an overview of techniques used to verify instrument performance, to verify model applicability to the spectrum of the sample under test, and to verify equivalence between the parameters calculated from the infrared measurement and the results of the primary test method measurement.

1.5 This practice teaches and recommends appropriate statistical tools, outlier detection methods, for determining whether the spectrum of the sample under test is a member of the population of spectra used for the analyzer calibration. The statistical tools are used to determine if the infrared measurement results in a valid property or parameter estimate.

1.6 The outlier detection methods do not define criteria to determine whether the sample or the instrument is the cause of an outlier measurement. Thus, the operator who is measuring samples on a routine basis will find criteria to determine that a spectral measurement lies outside the calibration, but will not have specific information on the cause of the outlier. This practice does suggest methods by which instrument performance tests can be used to indicate if the outlier methods are responding to changes in the instrument response.

1.7 This practice is not intended as a quantitative performance standard for the comparison of analyzers of different design.

1.8 Although this practice deals primarily with validation of infrared analyzers, the procedures and statistical tests described herein are also applicable to other types of analyzers which employ multivariate models.

1.9 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D1265 Practice for Sampling Liquefied Petroleum (LP) Gases, Manual Method

D3764 Practice for Validation of the Performance of Process Stream Analyzer Systems

D4057 Practice for Manual Sampling of Petroleum and Petroleum Products

D4177 Practice for Automatic Sampling of Petroleum and Petroleum Products

D6299 Practice for Applying Statistical Quality Assurance and Control Charting Techniques to Evaluate Analytical Measurement System Performance

D6708 Practice for Statistical Assessment and Improvement of Expected Agreement Between Two Test Methods that Purport to Measure the Same Property of a Material

[1] This practice is under the jurisdiction of ASTM Committee D02 on Petroleum Products, Liquid Fuels, and Lubricants and is the direct responsibility of Subcommittee D02.25 on Performance Assessment and Validation of Process Stream Analyzer Systems.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

D7278 Guide for Prediction of Analyzer Sample System Lag Times
D7453 Practice for Sampling of Petroleum Products for Analysis by Process Stream Analyzers and for Process Stream Analyzer System Validation
D7808 Practice for Determining the Site Precision of a Process Stream Analyzer on Process Stream Material
D7717 Practice for Preparing Volumetric Blends of Denatured Fuel Ethanol and Gasoline Blendstocks for Laboratory Analysis
E131 Terminology Relating to Molecular Spectroscopy
E275 Practice for Describing and Measuring Performance of Ultraviolet and Visible Spectrophotometers
E456 Terminology Relating to Quality and Statistics
E932 Practice for Describing and Measuring Performance of Dispersive Infrared Spectrometers
E1421 Practice for Describing and Measuring Performance of Fourier Transform Mid-Infrared (FT-MIR) Spectrometers: Level Zero and Level One Tests
E1655 Practices for Infrared Multivariate Quantitative Analysis
E1866 Guide for Establishing Spectrophotometer Performance Tests
E1944 Practice for Describing and Measuring Performance of Laboratory Fourier Transform Near-Infrared (FT-NIR) Spectrometers: Level Zero and Level One Tests

3. Terminology

3.1 *Definitions:*

3.1.1 For definitions of terms and symbols relating to IR spectroscopy, refer to Terminology E131.

3.1.2 For definitions of terms and symbols relating to multivariate calibration, refer to Practices E1655.

3.1.3 For definitions of terms relating to statistical quality control, refer to Practice D6299 and Terminology E456.

3.1.4 *between-method reproducibility (R_{XY}), n*—a quantitative expression of the random error associated with the difference between two results obtained by different operators using different apparatus and applying the two methods *X* and *Y*, respectively, each obtaining a single result on an identical test sample, when the methods have been assessed and an appropriate bias-correction has been applied in accordance with this practice; it is defined as the 95 % confidence limit for the difference between two such single and independent results. **D6708**

3.1.5 *control limits, n*—limits on a control chart which are used as criteria for signaling the need for action, or for judging whether a set of data does or does not indicate a state of statistical control. **E456**

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *action limit, n*—the limiting value from an instrument performance test, beyond which the analyzer is expected to produce potentially invalid results.

3.2.2 *analyzer, n*—all piping, hardware, computer, software, instrumentation and calibration model required to automatically perform analysis of a process or product stream.

3.2.3 *analyzer calibration, n*—see *multivariate calibration*.

3.2.4 *analyzer site precision, n*—a statistical measure of the expected long-term variability of analyzer results for samples whose spectra are neither outliers, nor nearest neighbor inliers.

3.2.5 *analyzer model, n*—see *multivariate model*.

3.2.6 *analyzer repeatability, n*—a statistical measure of the expected short-term variability of results produced by the analyzer for samples whose spectra are neither outliers nor nearest neighbor inliers.

3.2.7 *analyzer result, n*—the numerical estimate of a physical, chemical, or quality parameter produced by applying the calibration model to the spectral data collected by the analyzer.

3.2.8 *analyzer validation test, n*—see *validation test*.

3.2.9 *calibration transfer, n*—a method of applying a multivariate calibration developed on one analyzer to a different analyzer by mathematically modifying the calibration model or by instrument standardization.

3.2.10 *check sample, n*—a single, pure liquid hydrocarbon compound or a known, reproducible mixture of liquid hydrocarbon compounds whose spectrum is constant over time such that it can be used in a performance test.

3.2.11 *exponentially weighted moving average control chart, n*—a control chart based on the exponentially weighted average of individual observations from a system; the observations may be the differences between the analyzer result, and the result from the primary test method.

3.2.12 *individual observation control chart, n*—a control chart of individual observations from a system; the observations may be the differences between the analyzer result and the result from the primary test method.

3.2.13 *inlier, n*—see *nearest neighbor distance inlier*.

3.2.14 *inlier detection methods, n*—statistical tests which are conducted to determine if a spectrum resides within a region of the multivariate calibration space, which is sparsely populated.

3.2.15 *in-line probe, n*—a spectrophotometer cell installed in a process pipe or slip stream loop and connected to the analyzer by optical fibers.

3.2.16 *instrument, n*—spectrophotometer, associated electronics and computer, spectrophotometer cell and, if utilized, transfer optics.

3.2.17 *instrument standardization, n*—a procedure for standardizing the response of multiple instruments such that a common multivariate model is applicable for measurements conducted by these instruments, the standardization being accomplished by way of adjustment of the spectrophotometer hardware or by way of mathematical treatment of the collected spectra.

3.2.18 *line sample, n*—a process or product sample which is withdrawn from a sample port in accordance with Practices D1265, D4057, D4177, or D7453, whichever is applicable, during a period when the material flowing through the analyzer is of uniform quality and the analyzer result is essentially constant.

3.2.19 *moving range of two control chart, n*—a control chart that monitors the change in the absolute value of the difference between two successive differences of the analyzer result minus the result from the primary test method.

3.2.20 *multivariate calibration, n*—an analyzer calibration that relates the spectrum at multiple wavelengths or frequencies to the physical, chemical, or quality parameters.

3.2.21 *multivariate model, n*—a multivariate, mathematical rule or formula used to calculate physical, chemical, or quality parameters from the measured infrared spectrum.

3.2.22 *nearest neighbor distance inlier, n*—a spectrum residing within a gap in the multivariate calibration space, the result for which is subject to possible interpolation error.

3.2.23 *optical background, n*—the spectrum of radiation incident on a sample under test, typically obtained by measuring the radiation transmitted through the spectrophotometer cell when no sample is present, or when an optically thin or nonabsorbing liquid is present.

3.2.24 *optical reference filter, n*—an optical filter or other device which can be inserted into the optical path in the spectrophotometer or probe producing an absorption spectrum which is known to be constant over time, such that it can be used in place of a check or test sample in a performance test.

3.2.25 *outlier detection limits, n*—the limiting value for application of an outlier detection method to a spectrum, beyond which the spectrum represents an extrapolation of the calibration model.

3.2.26 *outlier detection methods, n*—statistical tests which are conducted to determine if the analysis of a spectrum using a multivariate model represents an interpolation of the model.

3.2.27 *outlier spectrum, n*—a spectrum whose analysis by a multivariate model represents an extrapolation of the model.

3.2.28 *performance test, n*—a test that verifies that the performance of the instrument is consistent with historical data and adequate to produce valid results.

3.2.29 *physical correction, n*—a type of post-processing where the correction made to the numerical value produced by the multivariate model is based on a separate physical measurement of, for example, sample density, sample path length, or particulate scattering.

3.2.30 *post-processing, v*—performing a mathematical operation on an intermediate analyzer result to produce the final result, including correcting for temperature effects, adding a mean property value of the analyzer calibration, and converting into appropriate units for reporting purposes.

3.2.31 *prediction deviations* (Δ), *n*—calculated differences (including algebraic sign) between predicted primary test method result and primary test result, defined as (PPTMR – PTMR).

3.2.31.1 *Discussion*—This is also referred to as prediction residuals in Practice D6708.

3.2.32 *pre-processing, v*—performing mathematical operations on raw spectral data prior to multivariate analysis or model development, such as selecting wave length regions, correcting for baseline, smoothing, mean centering, and assigning weights to certain spectral positions.

3.2.33 *Primary Test Method (PTM), n*—the analytical procedure used to generate the reference values against which the analyzer is both calibrated and validated; Practices E1655 uses the term reference method in place of the term primary test method.

3.2.34 *Primary Test Method Result (PTMR), n*—test result produced from an ASTM or other established standard test method that is accepted as the reference measure of a property.

3.2.35 *Predicted Primary Test Method Result (PPTMR), n*—result from the analyzer system, after application of any necessary correlation, that is interpreted as predictions of what the primary test method results would have been, if it was conducted on the same material.

3.2.36 *process analyzer system, n*—see *analyzer*.

3.2.37 *process analyzer validation samples, n*—see *validation samples*.

3.2.38 *spectrophotometer cell, n*—an apparatus which allows a liquid hydrocarbon to flow between two optical surfaces which are separated by a fixed distance, the sample path length, while simultaneously allowing light to pass through the liquid.

3.2.39 *test sample, n*—a process or product sample, or a mixture of process or product samples, which has a constant spectrum for a finite time period, and which can be used in a performance test; test samples and their spectra are generally not reproducible in the long term.

3.2.40 *transfer optics, n*—a device which allows movement of light from the spectrophotometer to a remote spectrophotometer cell and back to the spectrophotometer; transfer optics include optical fibers or other optical light pipes.

3.2.41 *validation samples, n*—samples that are used to compare the analyzer results to the primary test method results through the use of control charts and statistical tests; validation samples used in the initial validation may be line and test samples, whereas validation samples used in the periodic validation are line samples.

3.2.42 *validated result, n*—a result produced by the analyzer for a sample whose spectrum is neither an outlier nor a nearest neighbor inlier that is equivalent, within control limits to the result expected from the primary test method, so that the result can be used instead of the direct measurement of the sample by the primary test method.

3.2.43 *validation test, n*—a test performed on a validation sample that demonstrates that the result produced by the analyzer and the result produced by the primary test method are equivalent to within control limits.

4. Summary of Practice

4.1 This section describes, in summary form, the steps involved in the validation of an infrared analyzer over the long term. Before this practice may be undertaken, certain preconditions shall be satisfied. The preconditions are described in Section 7. This practice consists of four major procedures.

4.2 Each time a spectrum of a sample is collected using a laboratory or process analyzer, statistical tests are performed to verify that the multivariate model is applicable to the spectrum. Only spectra whose analysis represents interpolation of the multivariate model and which are sufficiently close to spectra in the calibration may be used in the analyzer validation.

4.3 When the analyzer is initially installed, or after major maintenance is concluded, performance tests are conducted to verify that the instrument is functioning properly. The intent of these tests is to provide a rapid indication of the state of the instrument. These tests are necessary but not sufficient to demonstrate valid analyzer results.

4.4 After the initial performance test is successfully completed, a probationary validation test is conducted on at least 15 samples that were not used in developing the multivariate model. The purpose of this probationary validation is to verify that the results produced by the analyzer (the PPTMRs) agree with the results from the primary test method (the PTMRs) to within user-defined limits for bias and precision. The PPTMRs and PTMRs are a compared using the statistical methodology of Practice D6708, recognizing that this is only a preliminary assessment. Precision and bias statistics on the prediction deviations (Δ) are generated for 15 samples whose spectra are not outliers nor nearest neighbor inliers, and the bias is assessed against pre-specified performance criteria. The system or subsystem performance is considered to be probationary validated for materials and property ranges representative of those used in the validation if the prediction deviations are in statistical control, and bias performance statistic meets pre-specified criterion providing that the spectra used in generating the results are neither outliers or nearest neighbor inliers.

4.5 After probationary validation is achieved, continued statistical quality control chart monitoring and analyses on Δ are carried out with new production samples to ensure ongoing prediction performance of the PPTMR meets the levels established from the probationary validation.

4.6 Once the total number of (PPTMR/PTMR/Δ) data sets for samples from probationary and continual validation reaches 30, a general validation is conducted using the statistical methodology of Practice D6708. The samples used in this general validation should only include those whose spectra are not outliers or nearest neighbor inliers relative to the multivariate model. The objective of the general validation is to demonstrate that the PPTMRs agree with the PTMRs to within user-defined limits for bias and precision on at least 30 samples covering a wider operating envelope, or, to confirm outcome from probationary validation with more accrued data.

4.7 During routine operation of the analyzer, validation tests are conducted on a regular, periodic basis to demonstrate that the analyzer results remain in statistical agreement with results for the primary test method. Prediction deviations (Δ) are monitored using statistical quality control charts at a frequency that is commensurate with the criticality of the application. Between validation tests, performance tests are conducted to verify that the instrument is performing in a consistent fashion.

5. Significance and Use

5.1 The primary purpose of this practice is to permit the user to validate numerical values produced by a multivariate, infrared or near-infrared laboratory or process (online or at-line) analyzer calibrated to measure a specific chemical concentration, chemical property, or physical property. *The validated analyzer results are expected to be statistically indistinguishable, over diverse samples whose spectra are neither outliers or nearest neighbor inliers, to those produced by the primary test method to within control limits established by control charts for the prespecified statistical confidence level.*

5.2 Procedures are described for verifying that the instrument, the model, and the analyzer system are stable and properly operating.

5.3 A multivariate analyzer system inherently utilizes a multivariate calibration model. In practice the model both implicitly and explicitly spans some subset of the population of all possible samples that could be in the complete multivariate sample space. The model is applicable only to samples that fall within the subset population used in the model construction. A sample measurement cannot be validated unless applicability is established. Applicability cannot be assumed.

5.3.1 Outlier detection methods are used to demonstrate applicability of the calibration model for the analysis of the process sample spectrum. The outlier detection limits are based on historical as well as theoretical criteria. The outlier detection methods are used to establish whether the results obtained by an analyzer are potentially valid. The validation procedures are based on mathematical test criteria that indicate whether the process sample spectrum is within the range spanned by the analyzer system calibration model. If the sample spectrum is an outlier, the analyzer result is invalid. If the sample spectrum is not an outlier, then the analyzer result is valid providing that all other requirements for validity are met. Additional, optional tests may be performed to determine if the process sample spectrum falls in a sparsely populated region of the multivariate space covered by the calibration set, too far from neighboring calibration spectra to ensure good interpolation. For example, such nearest neighbor tests are recommended if the calibration sample spectra are highly clustered.

5.3.2 This practice does not define mathematical criteria to determine from a spectroscopic measurement of a sample whether the sample, the model, or the instrument is the cause of an outlier measurement. Thus the operator who is measuring samples on a routine basis will find criteria in the outlier detection method to determine whether a sample measurement lies within the expected calibration space, but will not have specific information as to the cause of the outlier without additional testing.

6. Apparatus and Considerations for Quantitative IR Measurements

6.1 *Infrared or Near-Infrared Spectrophotometer:*

6.1.1 The analyzer covered by this practice is based on an infrared spectrophotometer, double-beam or single-beam, suitable for recording accurate measurements in the near-infrared

(780 nm to 2500 nm, 12820.5 cm^{-1} to 4000 cm^{-1}) or mid-infrared (4000 cm^{-1} to 400 cm^{-1}) regions, or both. The spectral range measured by the analyzer shall be the same or greater than that measured by the instrument used in collecting the spectral data upon which the multivariate calibration model is based. Complete descriptions of the instrumentation and procedures that are required for quantitative online process IR measurements are beyond the scope of this practice. Some general guidelines are given in Annex A1. (**Warning—**There are inherent dangers associated with the use of electrical instrumentation, online processes, and hydrocarbon materials. The users of this practice should have a practical knowledge of these hazards and employ appropriate safeguards.)

6.1.2 *In developing spectroscopic methods, it is the responsibility of the user to describe the instrumentation and the performance required to achieve the desired repeatability, reproducibility, and accuracy for the application.*

6.2 *Process Analyzer System*—The process analyzer system typically includes the spectrophotometer, transfer optics, the hardware for sample handling, the hardware for introduction of reference standards and solvents, the computer for controlling the spectrophotometer and calculating results, and the multivariate model. The system configuration should be compatible with the mid-infrared or near-infrared IR measurement and this practice.

6.3 *Collection of Line Samples:*

6.3.1 Withdraw line samples in accordance with accepted sampling methods as given by Practices D1265, D4057, D4177, or D7453, whichever is applicable. Flush the entire sample loop with the process stream sample prior to withdrawal of the line sample.

6.3.2 The intent of this practice is to collect samples that correspond directly to the spectra being collected by the analyzer. Collect the sample at a port close to the optical probe and at a time correlated with the collection of the sample spectrum. This practice requires that parameters that can impact the result also be recorded at the time of sample collection and the effect of these parameters is properly accounted for when comparing the results with the primary test method result. For a more detailed discussion of the various lag times that can influence the correspondence between the analyzer measurement and collection of line samples, see Practice D3764 and Guide D7278.

6.3.2.1 If line samples covering the composition and property range of interest cannot be acquired within a reasonable length of time once the validation process begins, consider using process-derived validation reference materials (VRMs) to extend the composition and property range of the validation sample set. A suitable process-derived VRM may simply be a batch of material obtained at a time prior to the start of the validation procedure, but one that was not used in calibrating either the analyzer or the primary test method. In general, the composition of a VRM used for validation should be similar to a composition that is anticipated for the process stream at some future time.

6.3.2.2 In cases where it is necessary to include the sample loop, or the sample conditioning unit, or both, in the validation procedure, VRMs should not be used to the exclusion of line sample unless it is practical to use the VRMs to validate both sample system and analyzer (this is generally not practical). The sample system can be excluded from the validation procedure if it is known that the sample system does not materially alter the composition or condition of the sample presented to the analyzer and if the sample system response time can be estimated with reasonable certainty. Guidance on how to meet these conditions is beyond the intended scope of this practice. If these conditions cannot be met and if VRMs are needed to extend the property and composition range of the validation set, it is recommended that the user conduct two probationary validations, one using line samples and the other using VRMs, to demonstrate that VRM procedure adequately reflects corresponding performance for actual process materials. Once demonstrated, the statistical quality control charting for continual validation can be done using VRM procedures, with a periodic line sample procedure mixed in over time to demonstrate that both procedures continue to provide similar and acceptable performance.

6.3.3 Sample storage for extended time periods is not recommended if there is likelihood that samples degrade with time. Chemical changes occurring during storage will cause changes in the spectrum, as well as changes in the property or quality parameter measured by the primary test method.

6.3.4 If possible, at the time of line sample withdrawal, collect sufficient quantity of sample material to allow for multiple measurements of the property or quality parameter by the primary test method, should such measurements be required.

7. Preconditions

7.1 Certain preconditions shall be met before this practice can be applied.

7.1.1 Install the analyzer in accordance with manufacturer's instructions.

7.1.2 Maintain analyzer and monitor per manufacturer's guidelines to assure proper peak shift and baseline management.

7.1.3 Develop and validate the multivariate calibration model used on the process analyzer using methods described in Practices E1655. If a calibration transfer method is used to transfer the model from one analyzer to another, verify the transferred model as described in Practices E1655.

NOTE 2—It is permissible to conduct the validation of the multivariate calibration model and the analyzer simultaneously using the same set of validation samples providing these samples meet the requirements of both Practices E1655 and this practice.

7.1.4 A quality assurance program for the primary test method is required in order to determine the usability of values generated by the primary test method in the validation of analyzer performance using this practice (see Section 8).

8. Reference Values and the Quality Assurance Program for the Primary Test Method

8.1 The property reference value against which analyzer results are compared during validation is established by applying the primary measurement method which was used in the

model development to line samples representing the process stream either directly, or after consistent treatment depending on the application.

8.1.1 If the line sample is treated prior to measurement by the primary method, such treatment should be done via procedures described in an appropriate ASTM standard such as Practice D7717. In the absence of an appropriate ASTM standard, the user shall document the treatment procedure in sufficient detail to ensure its consistent application.

8.2 A quality assurance program for the primary test method is required for values generated by this method to be used in analyzer validation. See Practice D6299 for reference.

8.2.1 Carefully check the laboratory apparatus used for primary test method measurement before these tests are performed to ensure compliance with the requirements of the primary test method.

8.2.2 Test control materials of known composition and quality on a regularly scheduled basis. Plot the primary test method results on control charts to ensure the long-term performance of the primary test. Individual values, exponentially weighted moving average, and moving range of two control charts are all recommended for charting the performance of the primary test method. Calculate the values for these control charts using equations given in Sections 12 and 13. Plot the differences between the primary test method result, and the expected value for the standard sample. Determine the historical precision of the primary test method from these regular tests, and compare it to published values for the method to determine if the test is within expected limits. Compare the historical precision to the analyzer precision using statistical tests.

9. Procedure

9.1 A flowchart for the steps involved in this practice, as it applies to process analyzers, is shown in Figs. 1-3.

9.2 *Initial Performance Tests:*

9.2.1 After the multivariate process analyzer has been installed (or reinstalled following major maintenance), check the performance of the instrument. Refer to manufacturer's instructions to ensure sufficient signal to noise ratio, peak positioning, and baseline management. The objective of the check is to determine that current performance of the instrument is consistent with performance which is known to produce valid analyses. Collect spectra of 20 check or test samples and analyze them using one or more of the Level 0, Level A, or Level B performance tests described in Annex A2 and Practice E1866.

9.2.2 Performance test results should be plotted on control charts and examined for trends. Such trend analysis may provide early warnings of possible analyzer problems. See Annex A2 and Practice D6299.

9.2.3 Compare the results for the initial performance tests to performance test action limits. These action limits may be based on historical data for the same tests, on simulations of the effects of performance changes on the analyzer results, or on a combination of historical and simulated data. Methods for establishing action limits are discussed in Annex A2 and Practice E1866.

9.2.3.1 If the performance test results are within action limits, then the procedure continues with the initial validation tests. If the performance test results are not within action limits, check installation, instrument standardization or calibration transfer, or combination thereof, and correct the cause of the inadequate performance. Repeat the initial performance tests.

9.2.3.2 If action limits for performance tests have not been established, use the results for the initial performance tests to generate an initial historical database against which future tests can be compared, and continue the validation procedure with the steps described in 9.3. In the absence of historical data or performance simulations, the performance of the instrument cannot be verified, but shall be assumed. Should the analyzer fail to validate, inadequate instrument performance could be responsible.

9.3 *Probationary Validation* (see Section 12 for details):

9.3.1 For an online or at-line process analyzer, once the initial performance tests are completed, collect spectra of 15 line and test samples and analyze them using the multivariate model. In order for the results to be used in the initial validation test, the spectra of the 15 line or test samples shall not be either outliers or nearest neighbor inliers (see Section 11 and Annex A3). Replace samples whose spectra are outliers or nearest neighbor inliers with other line or test samples.

9.3.2 Withdraw line samples from the process using methods described in Practices D1265, D4057, or D4177, whichever is applicable. The line sample shall correspond directly to the spectrum collected in 9.3.1.

9.3.3 For a laboratory analyzer, collect spectra of sampled line product and analyze them using the multivariate infrared method.

9.3.4 If appropriate, treat the line samples in a consistent fashion to produce treated line samples.

9.3.5 Analyze the line samples or treated line samples using the PTM.

9.3.6 Perform a preliminary Practice D6708 assessment of the agreement between the PPTMRs and the PTMRs. If there is insufficient variation among the 15 samples, conduct a level-specific probationary validation.

NOTE 3—If line samples covering the composition and property range of interest cannot be acquired within a reasonable length of time once the validation process begins, consider using either process-derived validation reference materials (VRMs) to extend the composition and property range of the validation sample set. A suitable process-derived VRM may simply be a batch of material obtained at a time prior to the start of the validation procedure which was not used in developing the multivariate calibration model nor for calibrating the primary test method. In general, the composition of a VRM used for validation should be similar to a composition that is anticipated for the process stream at some future time.

9.3.7 Compare values calculated by the analyzer to those obtained by the primary test method using statistical tests described in Section 12. If the values are in statistical control, and there is no significant bias, then the analyzer passes probationary validation and can be used to analyze line samples within the range over which the validation was conducted. If the values are not within statistical agreement, then the installation, instrument standardization or calibration

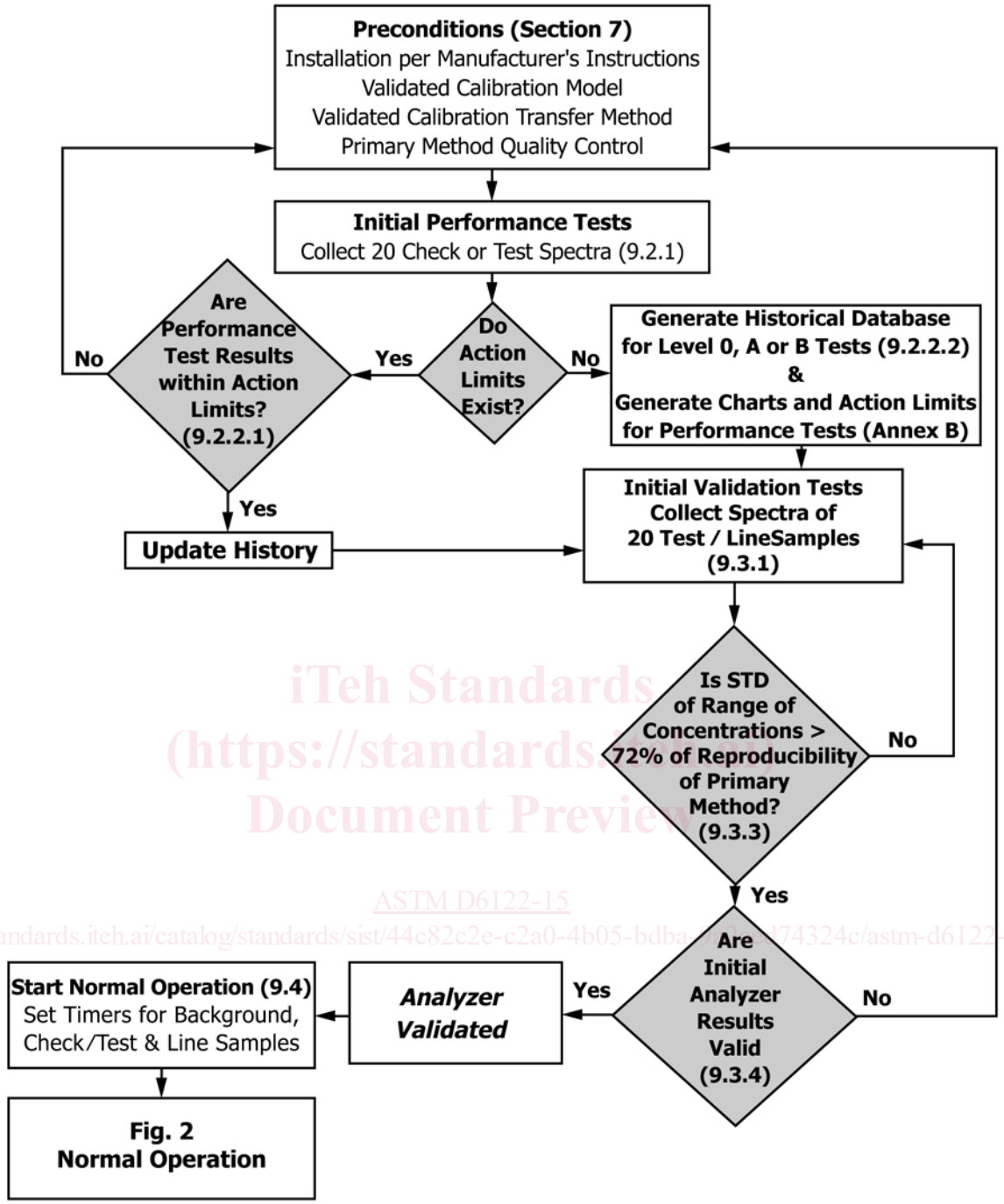

FIG. 1 Flowchart of Process Analyzer Validation Practice Initial Startup and Restart after Maintenance

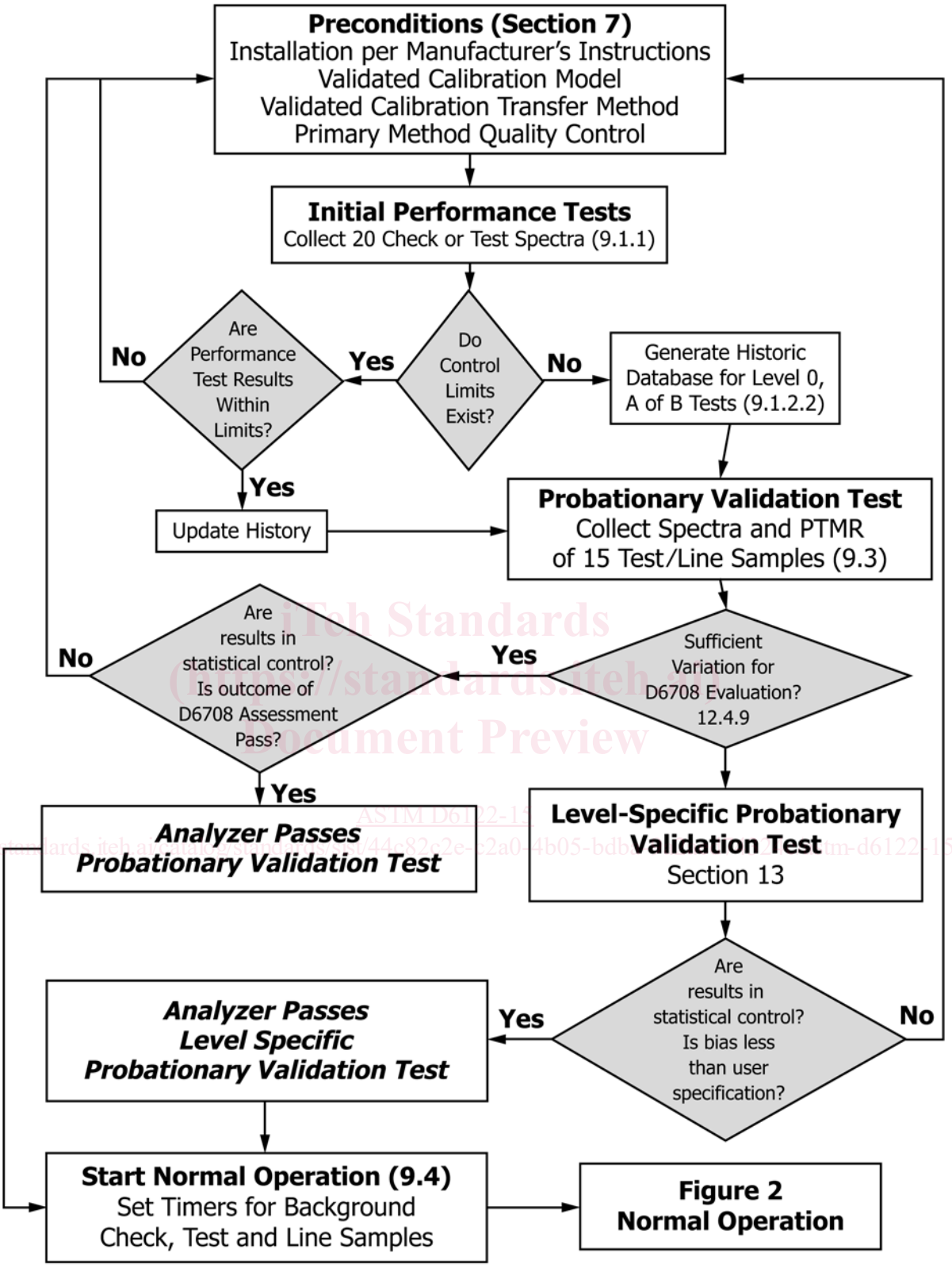

FIG. 1 Flowchart of Process Analyzer Validation Practice Initial Startup and Restart after Maintenance *(continued)*

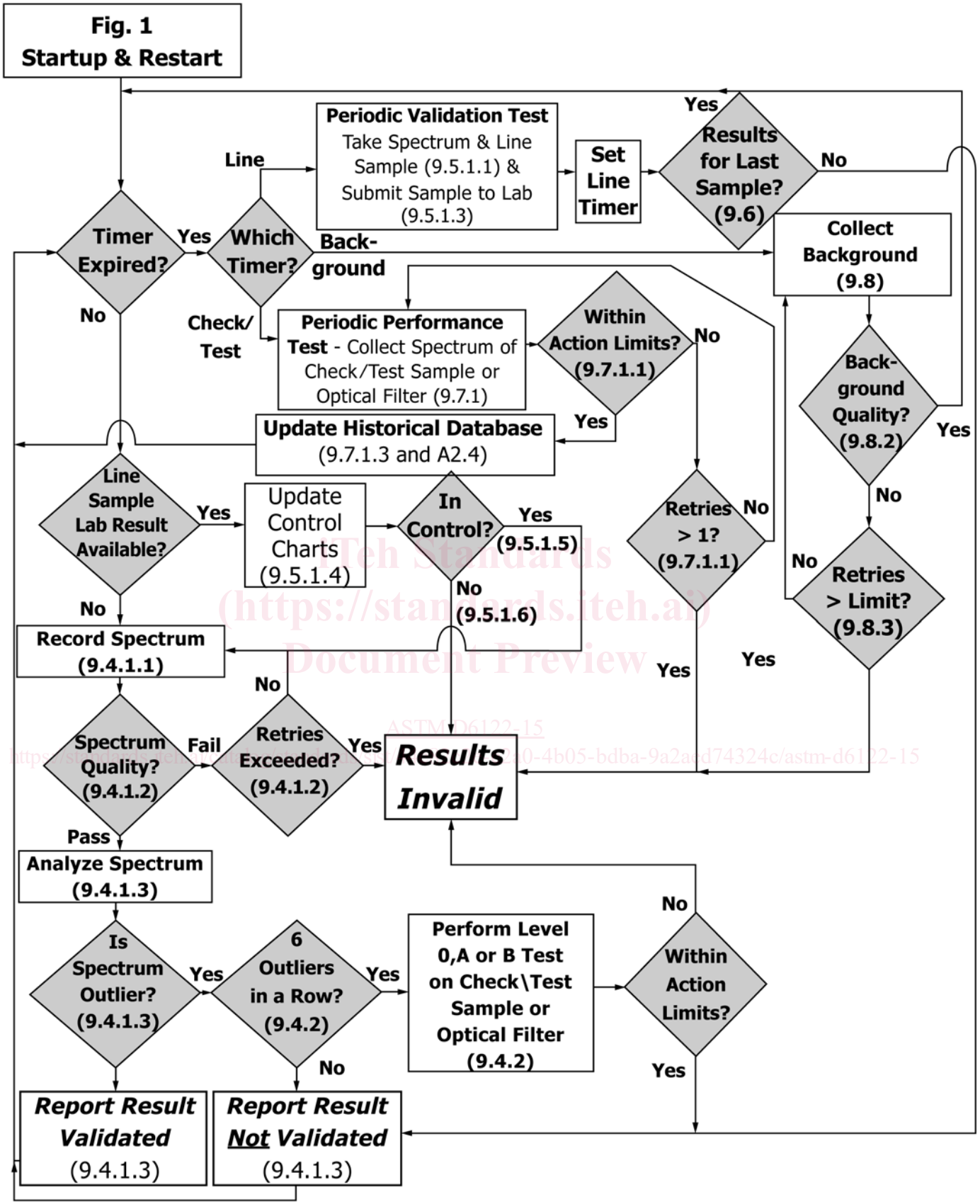

FIG. 2 Flowchart of Process Analyzer Validation Practice Normal Operation

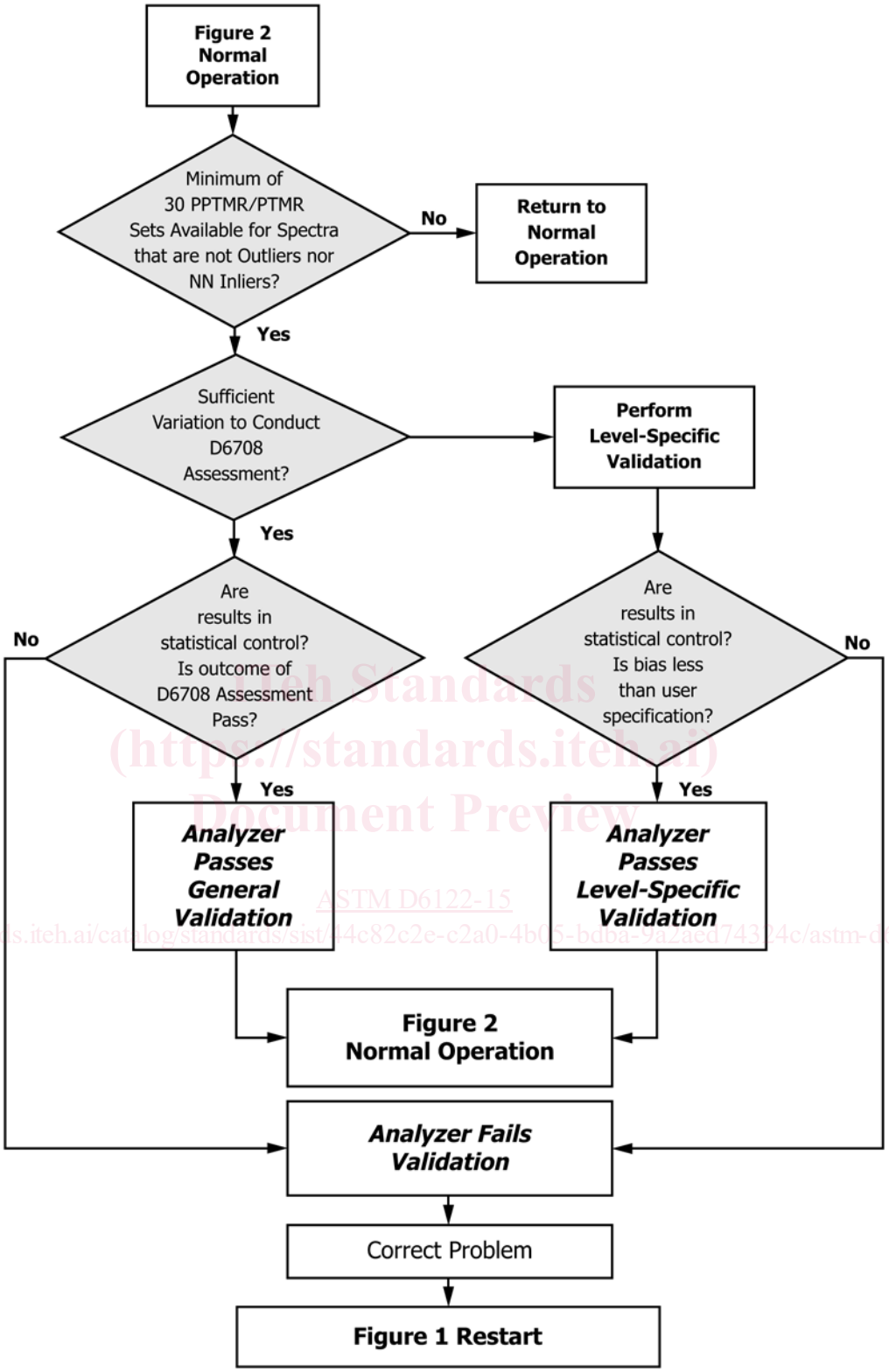

FIG. 3 Flowchart of Process Analyzer Validation Practice General Validation