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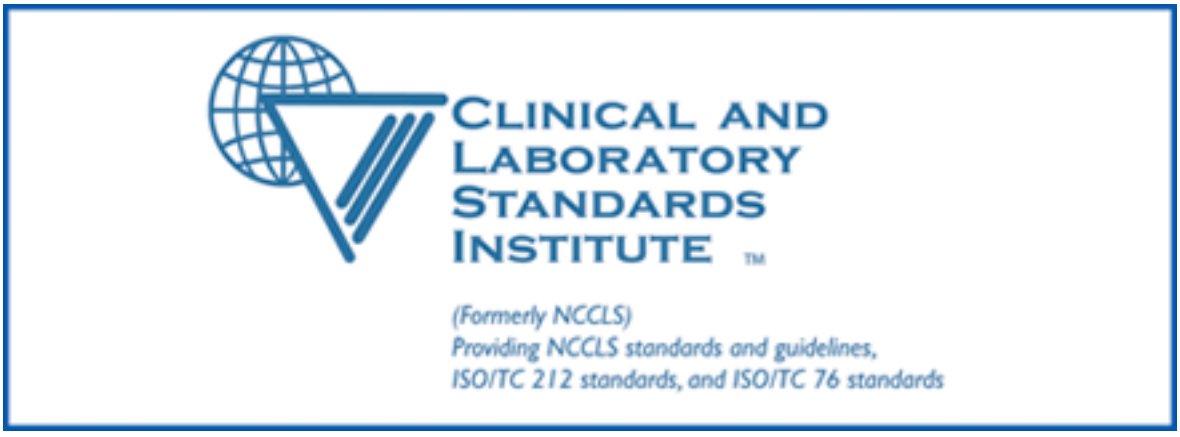
A Framework for NCCLS Evaluation Protocols; A Report



This report describes the different types of performance studies that are conducted to evaluate clinical assays.

A report developed by the NCCLS Area Committee on Evaluation Protocols

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A Framework for NCCLS Evaluation Protocols; A Report

Abstract

This report describes the different types of performance studies that are conducted to evaluate clinical assays: namely, validation, verification, and demonstration studies. Each evaluation protocol guideline is categorized with respect to its evaluation type. The tasks that comprise the path of workflow, which takes place when an assay is considered for use by a laboratory, are listed and explained. A recommendation for the data analysis portion of the evaluation is discussed, whereby the use of confidence intervals over hypothesis testing is recommended.

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Foreword

This report presents an overview of the relationships among evaluation experiments that are performed by manufacturers, by clinical laboratories, and/or that may be required by governmental agencies. It is the objective of the NCCLS Area Committee on Evaluation Protocols to provide recommendations for the assessment of laboratory test procedures in a way that defines good laboratory practices that are grounded on good scientific and statistical theory.

NCCLS evaluation protocols are primarily intended to be practical in their use in the clinical laboratory. All clinical laboratories must perform method evaluation studies prior to using a new or revised test system for reporting patient test results. The extent of a given study may vary considerably depending on the objectives of the laboratory, on resources available in the laboratory, and on information that may have been previously reported in technical literature by other laboratories.

NCCLS evaluation protocols are not intended to be so comprehensive as to provide the sole data on product testing and qualification on the part of manufacturers of *in vitro* diagnostic devices. There are many other studies that a manufacturer will perform during the research and development phases and during the manufacturing validation phase that are unique to the design of the test kit or test system and the manufacturing processes themselves. These special studies go beyond the scope of NCCLS evaluation protocols. However, it is appropriate that manufacturers use these NCCLS documents as a means of generating performance data for the final product in a form to which the laboratory can relate.

In addition to defining a framework for a family of evaluation studies that should result in greater consensus and standardization of practice, this report reviews two different approaches for statistical analysis of the results: tests of significance and the use of confidence interval estimates. The latter is preferred, so that the laboratorian focuses attention on the magnitude of an error assessment in the comparison to stated claims or stated requirements from a clinical perspective.

EP19 was originally conceived as a report and was primarily intended for use by evaluation protocols subcommittees. However, as draft copies were circulated during its preparation, some NCCLS users outside of the evaluation protocols area committee who reviewed the report found intrinsically valuable information in the document and suggested that it be made available as a guideline. The Area Committee on Evaluation Protocols concurred with users' recommendations and issued EP19 as a proposed-level consensus document. However, due to the limited input received on EP19-P during the public review and comment period, the area committee agreed that EP19 be reissued as a report, made available to all NCCLS users.

Key Words

Demonstration, evaluation protocol, validation, verification

The Quality System Approach

NCCLS subscribes to a quality system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents through a gap analysis. The approach is based on the model presented in the most current edition of NCCLS document HS1—*A Quality System Model for Health Care.* The quality system approach applies a core set of "quality system essentials (QSEs)," basic to any organization, to all operations in any healthcare service's path of workflow. The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The quality system essentials (QSEs) are:

QSEs

Documents & Records	Information Management
Organization	Occurrence Management
Personnel	Assessment
Equipment	Process Improvement
Purchasing & Inventory	Service & Satisfaction
Process Control	Facilities & Safety

EP19-R Addresses the Following Quality System Essentials (QSEs)

Documents & Records	Organization	Personnel	Equipment	Purchasing & Inventory	Process Control	Information Management	Occurrence Management	Assessment	Process Improvement	Service & Satisfaction	Facilities & Safety
					X						

Adapted from NCCLS document HS1—*A Quality System Model for Health Care.*

A Framework for NCCLS Evaluation Protocols; A Report

1 Introduction

It is the objective of the NCCLS Area Committee on Evaluation Protocols to provide recommendations for the assessment of laboratory test procedures in a way that defines good laboratory practices that are grounded on good science and statistical theory. These recommendations are primarily intended to be practical in their use in the clinical laboratory. They are not intended to be so comprehensive as to be the sole data on product testing and qualification on the part of manufacturers of *in vitro* diagnostic devices. However, it is appropriate that manufacturers use these documents as a means of generating performance data to which the laboratory can relate.

1.1 Purpose

It is recognized that laboratories may have different needs and purposes for conducting evaluation studies; they may have different resources to apply to an evaluation study; and there may be different performance requirements.

This report creates a framework that relates the scope and design of an evaluation study to the purpose of the study. The framework also integrates this hierarchy of evaluation studies with the amount of performance information that may be known prior to the study. (This is discussed in greater detail in Section 2, Scope.)

Finally, this report incorporates the fundamentals of a defined path of workflow[1-3] for an evaluation study as described in Section 4. Please refer to the most recent edition of NCCLS document HS1—*A Quality System Model for Health Care* for additional information. All evaluation studies, regardless of purpose and scope have certain key elements or steps in common. Key issues that have been sources of confusion are discussed in more detail in the appropriate steps in the overall process for an evaluation study.

1.2 Consensus on Statistical Application

Implied in the discussion of purpose is the requirement that there be a common understanding of the best approach in the application of statistics for data analysis and interpretation. Section 6.1 states that the use of confidence interval estimates of error is preferred over tests of statistical significance.[4-10] Confidence interval estimates reflect both the magnitude of an error as well as the uncertainty of that estimate, while tests of significance are based on a ratio of errors, so that the magnitude of the error may be lost in the final interpretation. It is recognized that in the clinical laboratory setting, the magnitude of the error due to a given effect is of greater importance than whether the error is "statistically" significant. The ultimate decision regarding the acceptability of the performance of a given test or product should be based on whether the magnitude of a given error is less than the medical or regulatory requirement.

1.3 Literature Citations

It is recommended that statistical methods, whether for experimental design, data analysis, or interpretation of data, be referenced from peer-reviewed journals and/or established reference textbooks. Several NCCLS guidelines have been published with little or no reference to the technical literature, and this should be corrected. New documents and those under development should be adequately referenced prior to the next stage in the consensus process. Existing documents should have appropriate references added at the time of their next review.

2 Scope

This report is intended for use by all constituent groups of NCCLS—clinical laboratory professionals, manufacturers, and governmental agencies—as a basis for arriving at a consensus for the need for different evaluation studies that are designed to meet different purposes.

NCCLS evaluation protocols are not intended to be so comprehensive as to provide the sole data on product testing and qualification on the part of manufacturers of *in vitro* diagnostic devices. There are many other studies that a manufacturer will perform during the research and development phases and during the manufacturing validation phase that are unique to the design of the test kit or test system and the manufacturing processes themselves. These special studies go beyond the scope of NCCLS evaluation protocols. However, it is appropriate that manufacturers use these recommendations as a means of generating performance data for the final product in a form to which the laboratory can relate.

3 Definitions[a]

Alpha level, *n* – The probability that one will reject the null hypothesis when it is true; **NOTE:** The alpha level is often set at 5 or 1 percent.

Confidence interval, *n* – An interval estimate of a population parameter computed so that the statement "the population parameter lies in this interval" will be true ... in a stated proportion of the times such statements are made.

Demonstration (study), *n* – A study performed by a laboratory to show that it is capable of using a test system to obtain expected performance.

Evaluation (study), *n* – A generic term for any study that measures the performance capabilities of an assay.

Hypothesis testing, *n* – ***In Statistics,*** the testing of two or more statistical hypotheses that are mutually exclusive so that exactly one hypothesis can be accepted at a specified confidence level.

Null hypothesis, *n* – The hypothesis of no difference or no differential effects beyond random variation.

Point estimate, *n* – A value that summarizes a set of data without accounting for the precision of the estimate (e.g., its uncertainty).

Validation, *n* – **1)** Confirmation, through the provision of objective evidence, that requirements for a specific intended use or application have been fulfilled; **NOTES:** a) The term "validated" is used to designate the corresponding status (*ISO 9000:2000*); b) The use conditions for validation can be real or simulated; **2)** A term used by the FDA for a study used to determine whether a test system meets user needs. ***(Federal Register: Part VII Dept. of Health and Human Services, FDA. 12 CFR Parts 808, 812, and 820. Rules and Regulations. October 7, 1996;61(195):52222–52601)***; **3)** The action {or process} of proving that a procedure, process, system, equipment, or method used works as expected and achieves the intended result.

Verification, *n* – **1)** Confirmation, through the provision of objective evidence, that specified requirements have been fulfilled; **NOTES:** a) The term "verified" is used to designate the corresponding status; b) Confirmation can comprise activities such as: performing alternative calculations; comparing a

[a] Some of these definitions are found in NCCLS document NRSCL8—*Terminology and Definitions for Use in NCCLS Documents.* For complete definitions and detailed source information, please refer to the most current edition of that document.

new design specification with a similar proven design specification; undertaking tests and demonstrations; and reviewing document prior to issue (*ISO 9000:2000*); **2)** A term used by the FDA for a study used to determine whether a test system meets specifications. ***(Federal Register: Part VII Dept. of Health and Human Services, FDA. 21 CFR Parts 808, 812, and 820. Rules and Regulations. October 7, 1996;61(195):52222–52601).***

4 Path of Workflow

The process for an evaluation study can be defined in terms of the four steps of the Deming quality improvement cycle: Plan, Do, Check, Act. In general application of this process for continuous quality improvement, the cycle is continuously repeated. However, in the situation where a method evaluation study is performed, the evaluation study is usually performed one time, prior to the use of a given procedure or test system for patient testing. In this way, the laboratory management and staff can know that the test system will meet their needs and the needs of their medical staff before it is used to test patient samples.

5 Phase 1: Plan

For a given study, it is essential that certain details be planned out to ensure that the study is sufficiently complete so that it has to be done only one time. The performance requirements should be defined before the evaluation has been initiated. These goals might be based on the manufacturer's claims on proficiency testing requirements, and on medical requirements defined by the clinicians who use the laboratory services. The scope of the study will impact on resources required. The type of test system will impact on training required, on technical expertise, and on the amount of "practice" required to ensure that the results reflect what will be obtained under routine use.

5.1 Define Requirements

The following requirements should be defined:

- managerial requirements, including cost, size, maintenance, sample size, etc.; and
- performance requirements, including total error, precision, bias, linearity, etc.

5.2 Select Test System to Be Evaluated

Selection of the test system for evaluation should be based on the requirements that have been defined. Any system that is to be considered a candidate must meet the practical requirements. The performance requirements may be used to select among the possible candidates.

5.3 Scope of the Evaluation Study

In order to select a protocol, the scope of the evaluation will be dependent on the purpose of the study. To differentiate among purposes, this report recommends the following.

5.3.1 Evaluate

This report recommends the use of the word "evaluate" as a generic term for any study that measures the performance capabilities of an assay. Several subclasses of evaluation studies are defined below. For the last three terms used below, "validate" is the most comprehensive, followed by "verify," and "demonstrate." "Establishment" studies are defined but not discussed further.

Evaluation protocols include:

- establishment studies (R&D);
- validation protocols;
- verification protocols; and
- demonstration protocols.

5.3.2 Establish Performance

The type of studies performed to "establish performance" are those that are performed by a manufacturer or research scientist in the research and development (R&D) or manufacturing phases to enable the manufacturer to define the parameters of the components and processes to achieve the intended product design. These are considered beyond the scope of NCCLS evaluation protocols, since in most cases, they are specific to the product design and manufacturing processes.

5.3.3 Validate

This term refers to evaluation studies that are performed to determine whether a test system meets defined user needs, where "user" is taken to mean the laboratory. This testing is performed either at a manufacturer or in an end-use laboratory. The term "external validation" is used if the evaluation is performed in an end user's environment. To validate a performance characteristic relative to user requirements, a statistically valid sample size must be included in the study design.

As alluded to in the introduction, the scope of a study may also be impacted by what is already known about the performance of a test system. For a new test system that has just been created by a manufacturer, it is necessary for the manufacturer to perform internal validation studies. After these have been shown to be successful, then the test system should be evaluated by an external validation by one or more selected end-user laboratories to see if the test system meets user requirements. This information may become part of the information used by the manufacturer to define the claims for performance. Once these claims have been defined, and the test system is available on the market for clinical use, then other laboratories may wish to perform external validation studies to confirm that the test system meets the claimed specifications.

5.3.4 Verify

This term refers to evaluation studies that are performed to determine whether certain specifications are met.[11] A manufacturer performs internal verification studies to confirm that the test system meets internal specifications that were based on laboratory requirements. A laboratory may perform verification studies to confirm that the test systems meet the specifications claimed by the manufacturer in the product literature (or product insert sheets). These verification studies might be referred to as "external verification studies." To verify a performance characteristic, a statistically valid sample size must be included in the study design.

After a number of these types of external studies (external verification or external validation) have been completed and published in the literature or by other communication mechanisms, one might conclude that the performance of such a test system is fairly well-known, and there is no need to validate or verify performance again. Nevertheless, it is incumbent for each laboratory to document that when such a test system is introduced into the laboratory, the laboratory staff is able to obtain "expected performance." Expected performance might be that based on performance documented elsewhere, such as by proficiency testing.

The distinction between verification and validation is shown in Figure 1, which describes a device design, development, and implementation process.

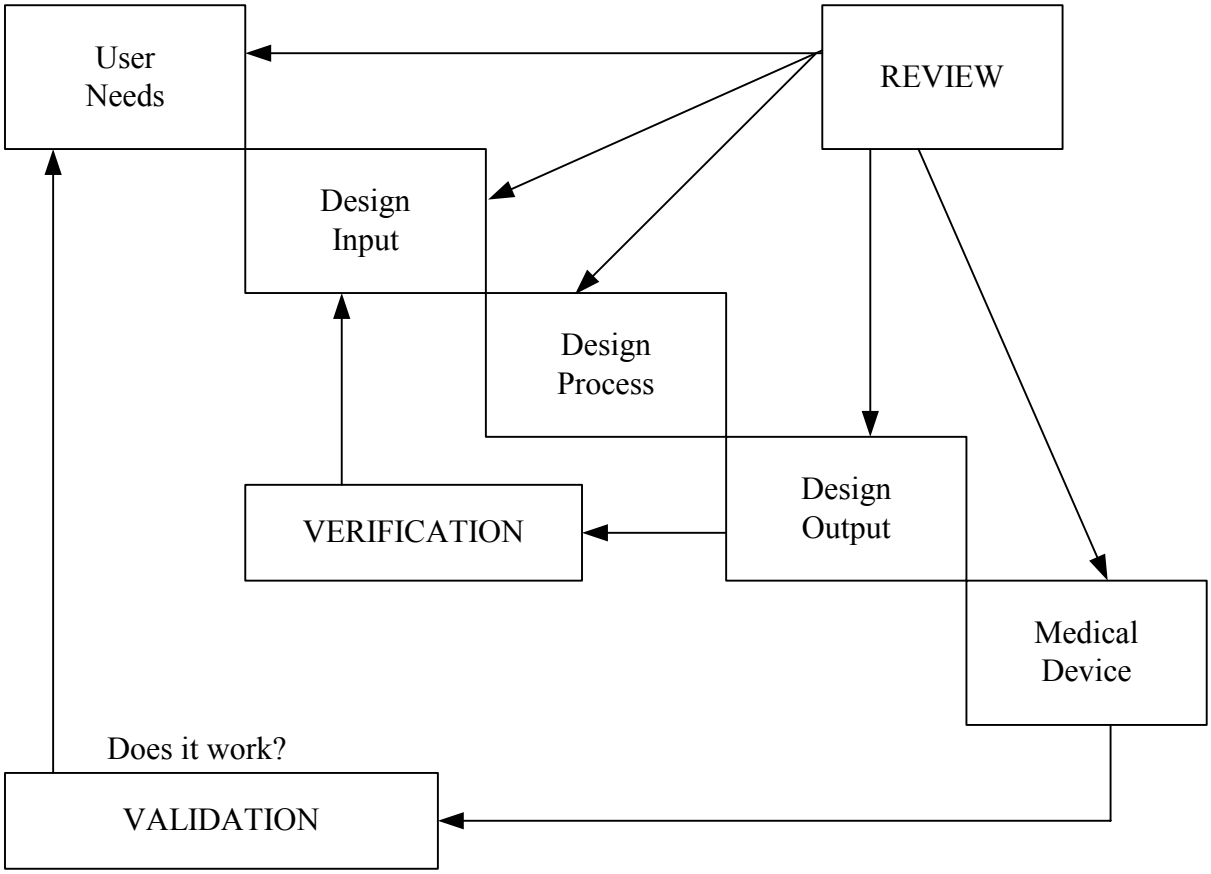

Figure 1. Design Acceptance. Adapted from the Federal Register: Part VII Dept. of Health and Human Services, FDA. 21 CFR Parts 808, 812, and 820. Rules and Regulations. October 7, 1996;61(195):52222–52601.

5.3.5 Demonstrate

This term refers to an evaluation study that is performed by a laboratory to enable them to show (demonstrate) that it is capable of using the test system to obtain expected performance. Examples of when demonstration evaluation would be performed include:

- **Demonstration of performance prior to implementation of a new test.**
- **Demonstration of performance after failure of proficiency testing.** In the case where a laboratory has failed proficiency testing, and after implementing suitable corrective actions, the laboratory can use this type of protocol to show that acceptable analytical performance is now being obtained.
- **Demonstration of performance to document technical competency of testing personnel.** This protocol may be used in the situation where laboratory staff uses this type of protocol to show abilities relative to the annual technical competency assessment.

Table 1 below shows a relationship between the study design and the amount of information that is known prior to performing such a study.

Table 1. Relationship Between Study Design and Information Known Prior to Study

Item to Test	Study
Design specifications	Verification
User requirements	Validation (Internal or External)
User requirements for specific laboratory	Demonstration

5.4 Selection of the Study Protocol

Once the scope of the evaluation study has been defined, the laboratory manager can select from appropriate NCCLS protocols to define the actual day-to-day tasks to be performed in the study. The laboratory staff should review this and perform several practice runs to ensure their awareness of the details of the study.

6 Phase 2: Perform Testing or "Do"

The actual testing details are described in the appropriate NCCLS evaluation protocol. Current protocols may not address all purposes and scopes as discussed above. Table 2 shows a summary of how current protocols may be related to the framework described in this document. Please refer to the appropriate document for more details.

Table 2. Current NCCLS Evaluation Protocols

Guideline	Title	Purpose*
EP5	Evaluation of Precision Performance	Val, Ver
EP6	Evaluation of the Linearity of Quantitative Analytical Methods	Val, Ver, Demo
EP7	Interference Testing	Val, Ver
EP9	Method Comparison and Bias Estimation Using Patient Samples	Val, Ver
EP10	Preliminary Evaluation of Quantitative Clinical Laboratory Methods	Demo
EP12	Evaluation of Qualitative Test Performance	Val, Ver, Demo
EP14	Evaluation of Matrix Effects	Val, Ver
EP15	User Demonstration of Performance for Precision and Accuracy	Demo
EP18	Unit-Use Testing	N/A
EP21	Total Error for Clinical Laboratory Methods	Val, Ver, Demo

*Val = "validate," Ver = "verify," and Demo = "demonstrate."

A key element in any evaluation is the application of statistics, both in terms of study design and in terms of result summarization to facilitate interpretation. Applications of statistics in study design are incorporated into each protocol. Applications of statistical techniques for proper interpretation of results are discussed in the next section.

6.1 Confidence Intervals Versus Hypothesis Testing

All scientific investigations have, or should have, a goal. Often, a study involves measurements that exhibit variation. With variation present, a statistically planned experiment is required to answer the question raised by the goal. Figure 2 shows a flow chart of the experimentation process. Table 3 shows that different goals lead to different data analysis methods. Thus, a goal can be either to answer a question with a yes/no response (e.g., verify) or to characterize something by estimating its value. For example, one can ask whether a new cholesterol method versus the reference method has a slope detectably different from one. Statistically, this goal results in use of a hypothesis test. Alternatively, one

can ask what is the actual slope of the new cholesterol method versus the reference method. Statistically, this results in estimating the slope and its confidence interval.

The purpose of this section is to compare the salient features of these two statistical procedures. The focus shall be on information content, ease of use, reliability, and interchangeability. This document is not a tutorial on how to perform these methods.

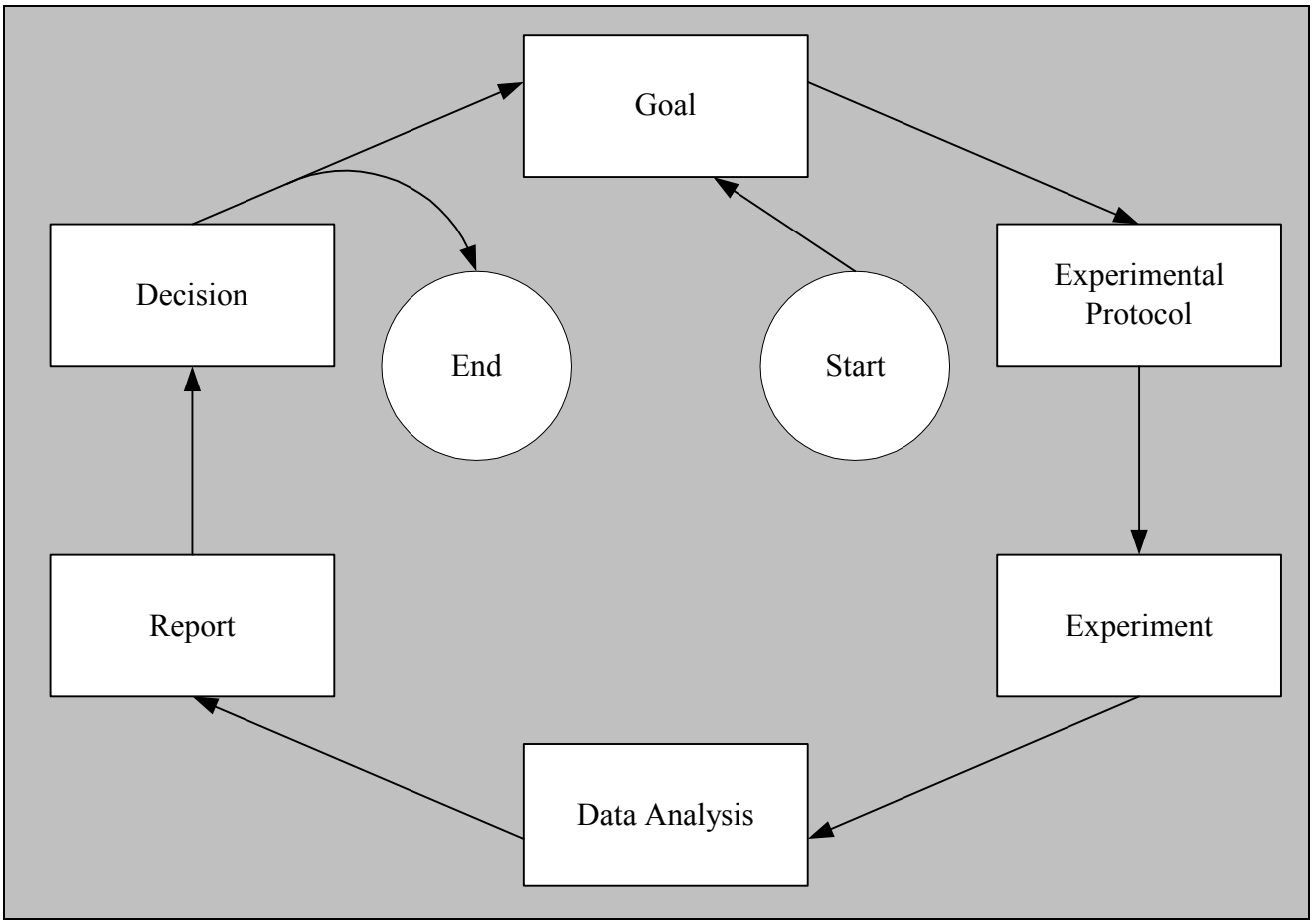

Figure 2. Flow Chart of the Experimental Process

Table 3. How Different Goals are Achieved Statistically

Goal	Data Analysis Method	Examples
Verify (yes/no)	Hypothesis Test	t-test F-test
Characterize	Estimation	Point Estimate Confidence Interval Prediction Interval Tolerance Interval

6.2 Hypothesis Tests

Hypothesis tests entail the following steps:

- State the null hypothesis.
  - — state the alternative hypothesis
  - — calculate the sample size
- Estimate the parameter.
- Perform the test.

The steps indented with a dash are often omitted, largely because they are difficult for nonstatisticians. Thus, the ease of use of the complete hypothesis test is low. The information content is also low, because one has dichotomized the result of a continuous variable. For example, using a hypothesis test one would answer "yes" to the question, "Is the patient hyperglycemic?" regardless of whether the glucose value was 150 or 500 mg/dL. People informally recognize this shortcoming of hypothesis testing by trying to attach different significance to different p values, such as "P = 0.03 is borderline" and "P less than 0.001 is highly significant." The problem with this approach is it is difficult to interpret values of P closer to each other (e.g., P = 0.002 vs. P = 0.009). Thus, the P scale, in spite of being continuous, is mainly interpreted as a categorical scale, often with only the two states, significant or not significant.

Reliability of the result will be high if all steps are followed and undetermined if the indented steps are omitted. This latter point can be shown by the following example. The question asked is: Does bilirubin interfere in a cholesterol assay? The hypothesis test procedure above is followed whereby the indented steps are skipped. In this example, the null hypothesis is "no interference" and the alpha level is 0.05. Assume the test result is nonsignificant (P greater than 0.05). The result is "no bilirubin interference" or, more correctly, "no bilirubin interference detected." Yet, assume that a 95% confidence interval was also calculated, and it was found that it covered –23 to 25 mg/dL. This means that bilirubin interference could be as high as 25 mg/dL. Hence, the reliability of the hypothesis test, with the indented steps of the procedure omitted, is low. Specifically, the possibility of false-negative results is left open.

6.3 Confidence Intervals

Confidence intervals shall be discussed; note that the discussion also applies to prediction and tolerance intervals. Confidence intervals entail the following steps:

- — State either the desired length of the confidence interval or deviation from target that one does not wish to exceed.
- State the alpha level.
  - — Calculate the sample size.
- Estimate the parameter.
- Calculate the confidence interval.

Once again, the intended steps are not always followed. Yet, even if one does not specify the deviation from target that one does not wish to exceed, the calculation of the confidence interval gives this

information, albeit respectively. Ease of use is similar to hypothesis testing, since in both procedures steps are omitted.

An advantage of using a confidence interval is that the parameter estimate and interval are on a continuous scale in the original units which provides more information than a yes/no response. Moreover, the length of the confidence interval affords a measure of the result's reliability. Reliability and clinical importance can be judged simultaneously. With either a hypothesis test or confidence interval, one needs to estimate the parameter (the point estimate). However, with a hypothesis test this estimate is incidental to the hypothesis test, whereas it is a key part of the confidence interval.

In many cases one can perform both procedures using data from the same experiment, but it is not always clear that this is meaningful. For example, to assess linearity, one can use a hypothesis test (lack of fit) to detect the presence of nonlinearity. There is no commonly performed confidence interval procedure that corresponds to this. On the other hand, one can estimate with a confidence interval the magnitude due to nonlinearity at a specific concentration level. In a sense, different questions are being answered (e.g., Is there global nonlinearity vs. the magnitude of nonlinearity at a specific concentration level?). Considering these questions up front is recommended as a means of deciding which statistical method to select.

For both procedures, discussing the necessary steps common to either method, checking the data for outliers, assuming a certain distribution, or any other step required by the estimation procedure have been omitted. This leads to a caution. With the additional information that is provided by a confidence interval, one may feel more secure in making decisions. Yet, a confidence interval will be accurate only if all required assumptions are true. The most important assumption and the one that is the most difficult to verify is that "the data are a representative sample from the population about which interferences are desired." For example, if one wishes to make a decision about the quality of results of an assay, one would perform an evaluation. If the assay is run on a random access analyzer routinely, and one performs the evaluation in a batch mode, the data will not be a representative sample. A famous example involves estimation of the solar unit by well-known scientists over a one-hundred-year period. Although each estimate had a confidence interval, each scientist's confidence interval failed to overlap the confidence interval of his predecessor.[12]

Most scientists recognize the importance of the assumption of representative data by using judgment in interpreting results and are thus aware of the syndrome *statistics on, brain off*.

Finally, it is recommended to display results graphically where possible. An example of a graphical display of confidence intervals for interference studies is shown below (Figure 3), taken from the most current version of NCCLS document EP7—*Interference Testing in Clinical Chemistry*.

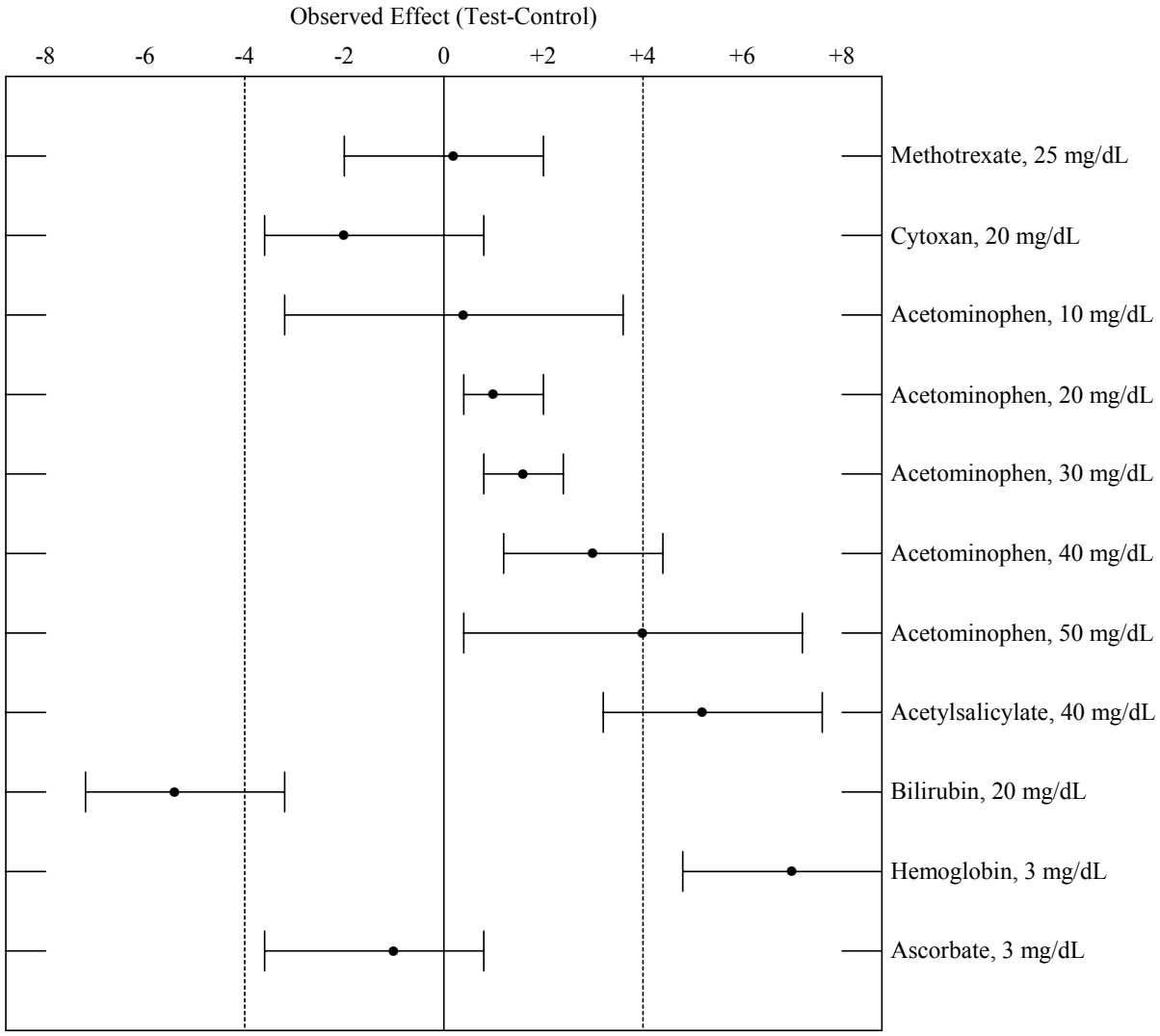

Figure 3. Graphical Display of Confidence Intervals

7 Phase 3: Check (and Communicate Conclusion)

All evaluation studies require some type of decision-making step, either to compare to the manufacturer's claims for an external verification study, or to compare to user requirements for an external validation study. In a demonstration study, one can compare to either the manufacturer's claims or to other sources of expected performance. This step should be described explicitly in each evaluation guideline or protocol.

Once the assessment of performance has been made, then the conclusion must be communicated. There are many parties that need to know the conclusion:

- laboratory staff;
- purchasing department;
- manufacturer; and
- medical staff

to name a few, and perhaps in that order.

8 Phase 4: Implement or Act

The actual evaluation process is not completed until the new test system has been implemented. This is the sole reason for performing the studies in the first place, except perhaps for those few academic research-oriented evaluations.

The implementation phase should describe:

- establishment of supply process;
- training of other laboratory staff;
- definition of the maintenance procedure;
- definition and establishment of the QC program (to monitor implementation);
- integration to the LIS system;
- notification to the medical staff; and
- feedback process from the medical staff.

9 Conclusion

It is essential that the clinical laboratory community (manufacturer, professional, and government) speak a common language with regard to the whole process of an evaluation study, which entails

- planning;
- performing the studies;
- analyzing the data and interpreting the results;
- reporting the results, conclusions, and recommendations;
- implementing the new test system;
- the different objectives for evaluations and how these lead to studies of different scope and design; and
- the appropriate use of statistics for data analysis and interpretation.

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Related NCCLS Publications*

EP5-A **Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (1999).** This document provides guidance for designing an experiment to evaluate the precision performance of clinical chemistry devices; recommendations on comparing the resulting precision estimates with manufacturer's precision performance claims and determining when such comparisons are valid; as well as manufacturer's guidelines for establishing claims.

EP6-P2 **Evaluation of the Linearity of Quantitative Analytical Methods; Proposed Guideline—Second Edition (2001).** This document provides guidelines for characterizing the linearity of a method during a method evaluation; for checking linearity as part of routine quality assurance; and for determining and stating a manufacturer's claim for linear range.

EP7-P **Interference Testing in Clinical Chemistry; Proposed Guideline (1986).** This document provides background information and procedures for characterizing the effects of interfering substances on test results.

EP9-A **Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (1995).** This document addresses procedures for determining the bias between two clinical methods or devices and for the design of a method comparison experiment using split patient samples and data analysis.

EP10-A **Preliminary Evaluation of Quantitative Clinical Laboratory Methods; Approved Guideline (1998).** This document addresses experimental design and data analysis for preliminary evaluation of the performance of an analytical method or device.

EP12-P **User Protocol for Evaluation of Qualitative Test Performance; Proposed Guideline (2000).** This document contains guidelines that optimize the experimental design for the evaluation of qualitative tests to better measure performance and provide a structured data analysis.

EP14-A **Evaluation of Matrix Effects; Approved Guideline (2001).** This document provides guidance for evaluating the error or bias in analyte measurements that results from the sample matrix (physiological or artificial) when two analytical methods are compared.

EP15-A **User Demonstration of Performance for Precision and Accuracy; Approved Guideline (2001).** This document demonstrates method precision and accuracy for laboratory analyte determinations, utilizing a protocol designed to be completed within five or fewer working days.

EP18-P **Quality Management for Unit-Use Testing; Proposed Guideline (1999).** This document recommends a quality management system for unit-use devices that will aid in the identification, understanding, and management of sources of error and help to ensure correct results. It is targeted for those involved in the supervision of laboratory-testing quality management, and it addresses issues related to specimen collection through reporting of test results.

* Proposed- and tentative-level documents are being advanced through the NCCLS consensus process; therefore, readers should refer to the most recent editions.

Related NCCLS Publications (Continued)

NRSCL8-A **Terminology and Definitions for Use in NCCLS Documents; Approved Standard (1998).** This document provides standard definitions for use in NCCLS standards and guidelines, and for submitting candidate reference methods and materials to the National Reference System for the Clinical Laboratory (NRSCL).

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