Quality Assurance: Are Laboratories Assuring, Assessing, or Assuming the Quality of Clinical Testing Today?

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Abstract: Quality assurance implies making certain, guaranteeing the attainment of quality. Do laboratories actually guarantee the quality of testing services today? If not, what is the purpose of quality assurance plans, programs, and practices? Have laboratories even defined the quality to be achieved for each test? If not, how can quality be guaranteed? Do current efforts in assessing quality provide for real-time control that will guarantee quality? If not, are laboratories just assuming that measuring quality will somehow make it happen?

Even analytical quality, which is fundamental for the core production processes of any laboratory, is mainly assessed and assumed, not assured. Problems include the lack of well defined quality requirements, inadequate method performance, poorly designed statistical control procedures, misguided quality control instructions and recommendations, insufficient technical quality management skills, reduced operator skills, and delays in implementing of laboratory regulations.

Quality assurance should be understood, not as a component, but as the outcome of a quality management process that includes quality planning, quality laboratory practices, quality control, quality assessment, and quality improvement, all linked together and guided by quality goals and customer requirements, and applied to the total testing process. In the future, automation and computerization will be necessary to manage the quality of centralized and distributed laboratory testing. Analytical quality will be guaranteed through on-line or on-board quality control. Other critical quality characteristics will need real-time monitors and control mechanisms to guarantee quality if process failures cannot be prevented.

Introduction

Quality Assurance (QA) has many definitions, but the expectation of customers and consumers of health care services is that quality should be certain. This implies guaranteeing the attainment of quality. QA sounds right, but are laboratories actually doing it right? Do current laboratory QA practices guarantee quality?

Guaranteeing quality presumes that laboratories know the quality that needs to be achieved. Have laboratories even defined quality requirements for critical characteristics such as analytical quality? Do laboratories know how to use quality requirements to establish the necessary process specifications? If not, how can quality be guaranteed?

Guaranteeing quality requires measurements to assess process performance and to control process output. Do initial method validation studies and periodic verification checks assure that daily quality is satisfactory? Is the four month cycle of proficiency testing adequate for assuring daily quality? Does periodic monitoring of quality indicators and outcome measures assure that daily quality is satisfactory? Are

internal process control procedures capable of detecting problems and assuring that daily quality is satisfactory? If not, are laboratories just assuming that this periodic measuring and monitoring of quality somehow guarantees quality in daily operations?

In my opinion, current QA practices mainly emphasize the assessment or measurement of quality, assuming (maybe "hoping" is a better word) that this interest and attention will work some magic to make quality happen. Laboratories need to recognize that quality assurance is actually the outcome of a quality management process that includes quality planning, quality laboratory practices, quality control, quality assessment, and quality improvement, all linked together and guided by quality goals and customer requirements.[1] This quality management process should be applied to the total testing process whenever possible and to critical steps when necessary.

I expect that my opinion about the state of laboratory quality assurance may not agree with other views presented here, so let me identify some of the issues that concern me. I will focus on analytical quality assurance here, knowing that others will focus on pre-analytical and post-analytical problems.

Analytical Quality Assurance

Analytical quality is fundamental to the core production processes of all laboratories. Problems that prevent the assurance of analytical quality include the lack of well defined quality requirements, inadequate method performance, poorly designed statistical control procedures, misguided quality control instructions and recommendations, insufficient technical quality management skills, reduced operator skills, and delays in implementing laboratory regulations.

Lack of well defined quality requirements

What is the proper way to define quality requirements for analytical performance? As an example of the current difficulties, consider the quality goals, requirements, and specifications for cholesterol. In the U.S., a total error requirement of 10% has been defined as the acceptability criterion for CLIA '88 proficiency testing (PT),[2] whereas the National Cholesterol Education Program (NCEP) has specified an allowable coefficient of variation (CV) of 3%, an allowable bias of 3%, and a decision interval for test interpretation corresponding to 20% at a decision level of 200 mg/dL.[3] For comparison, a European group has defined a precision goal of 2.7% and a bias goal of 4.1% based on the observed individual biological variation of about 6.5%.[4]

Laboratorians are often confused by all the different types of quality goals, requirements, and specifications that are being recommended. Some of these are test outcome criteria (medically significant change, allowable total error) and others are method performance specifications (allowable standard deviations, allowable bias). They all assume a stable measurement process, i.e., there is no need for internal quality control, or analytical quality assurance, because no problems are expected. If this assumption of stable performance is not correct, then it follows that these recommendations may not be correct for applications in real laboratories where problems do occur.

I suggest that relationships do exist between these various types of goals, requirements, and specifications and that a systems approach is needed to understand

and apply them. For example: medical and analytical outcome criteria share many similarities; both can be expressed as changes that are important or significant, and both can be understood as confidence intervals that provide bounds for the maximum deviation of a test result. Both can be translated into operating specifications for imprecision, inaccuracy, and quality control to manage the daily operation of laboratory testing processes.[5,6] Thus, a system can be defined as shown in Figure 1 to relate outcome criteria to the specifications needed to manage or operate laboratory testing processes, as well as to other aspects of laboratory quality management. The bottom line in this system is the definition of operating specifications for imprecision, inaccuracy, and the control rules and number of control measurements needed at the bench level to assure the desired analytical quality will be achieved in routine service.

Inadequate method performance

Ross and Lawson recently summarized the *state of the art* precision performance based on 1500 laboratories participating in the 1990 College of American Pathologists Quality Assurance Service.[7] In comparison with the analytical goals for imprecision based on biological variation, they concluded that these goals for precision were not met for most of the analytes studied and the need for method improvements continues.

A similar comparison has been made to the operating specifications derived from CLIA PT criteria.[8] For sodium, for example, where the CLIA PT total error requirement is 4 mmol/L or 3.08% at a level of 130 mmol/L, the allowable imprecision for 90% assurance of analytical quality is 0.6% to 0.8%. Less than 20% of laboratories are able to provide that performance; hence, sodium shows up as one of the most problematic tests on PT surveys. Only potassium (of the 19 tests studied) shows the precision performance that is necessary to guarantee analytical quality in most laboratories.[8]. For many others, improvement in analytical imprecision is needed if laboratories are to guarantee the analytical quality required by CLIA PT criteria, as well as current biologic goals.

Poorly designed statistical QC procedures

The QC procedures implemented in most laboratories are based on general recommendations or practice guidelines, rather than quantitative planning that considers the quality required for each test, the precision and accuracy observed for the particular method, and the sensitivity of the particular control rules and the low numbers of control measurements per run (2-6) that are recommended today.

Problems of high false rejection (false alarms) or low error detection may occur because of the inherent performance characteristics of different decision criteria and different numbers of control measurements. Figure 2 shows power curves for commonly used control rules and numbers of control measurements (N) that are practical in laboratories today. Note that these are *S-shaped* curves that show very low probabilities of rejecting runs when errors are small (multiples of the method standard deviation of 2 or less). Note also that some of these curves indicate high levels of false rejections (shown by the y-intercepts), i.e., rejections even when there are no errors except for the inherent imprecision of the measurement procedure. Common use of 2 SD limits on Levey-Jennings charts is expected to cause a false rejection rate of about 9% when N=2 and

Figure 1. Systems view of Analytical Quality Assurance (AQA)

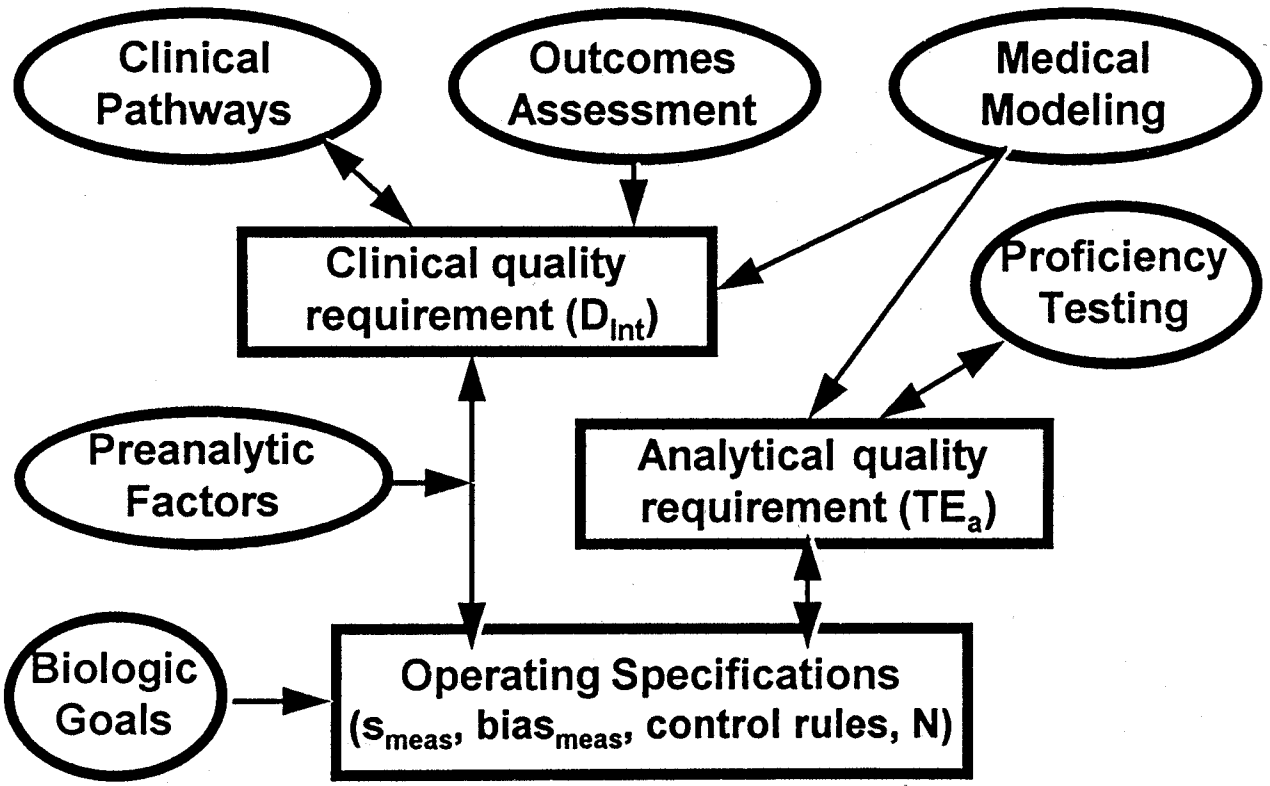

Figure 1

Figure 2. Performance of common QC procedures

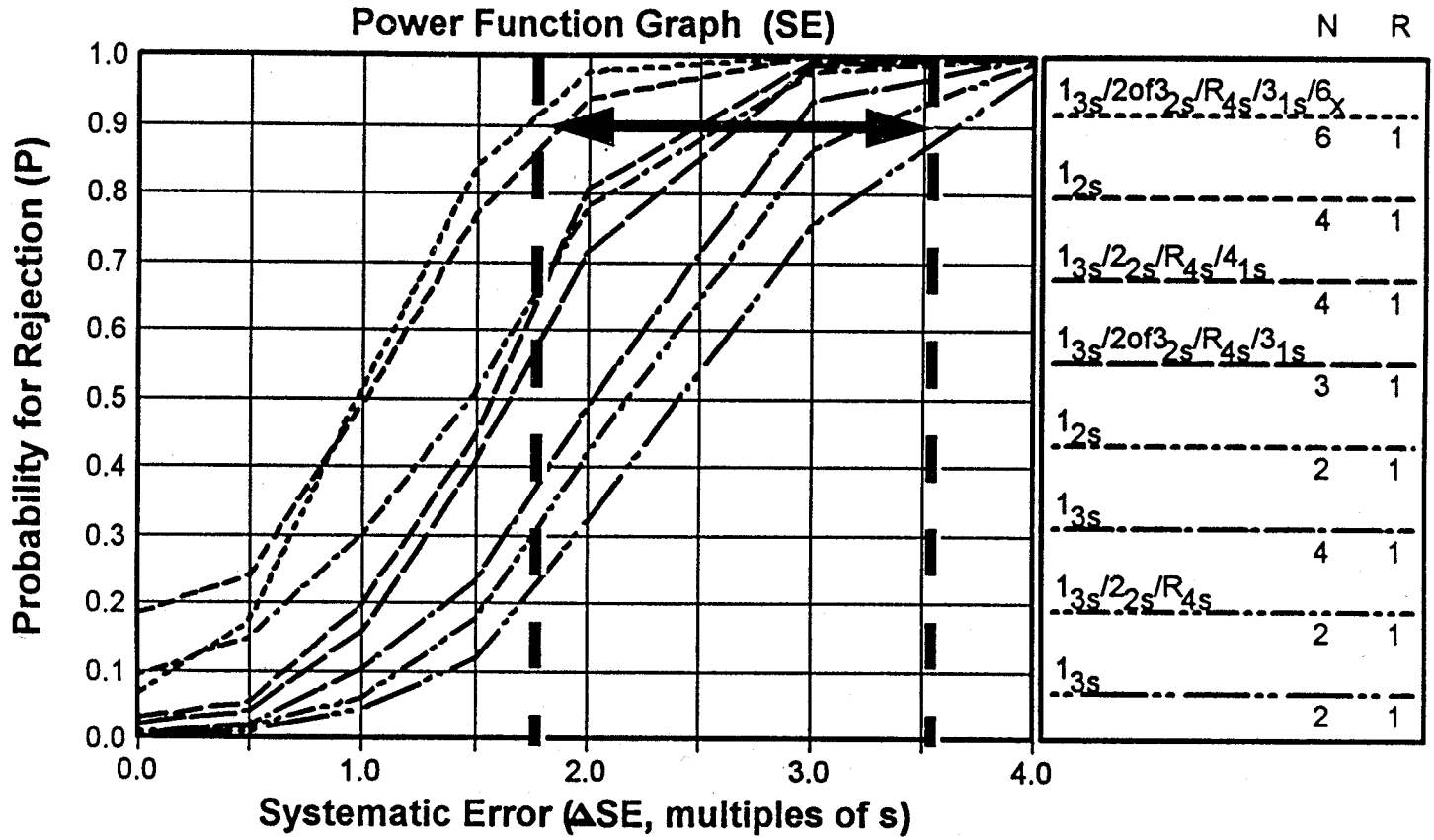

Figure 2

about 18% when N=4, i.e., nearly 10-20% of analytical runs would be falsely rejected by common QC practices. Ideally, the selected QC procedure should keep false rejections low (0-5%) and error detection high (90% or greater). For common QC procedures, this means that systematic errors may be as large as 1.8 to 3.7 times the size of the standard deviation of the measurement procedure before they are detected with the desired certainty.

Misguided quality control instructions and recommendations

Laboratories need to establish appropriate QC acceptability criteria to meet CLIA requirements for quality control. Guidelines presented in workshops, conferences, and published in the literature need to be evaluated quantitatively to validate their appropriateness for assuring analytical quality. Such guidelines may include recommendations for using statistical, fixed, and clinical control limits, without providing any information about the error detection and false rejection characteristics of the resulting QC procedure. Validation studies indicate that many current QC guidelines and recommendations are inadequate for assuring the quality required by CLIA PT criteria.[9,10]

Consider a glucose test, for example, where the method has an observed imprecision of 2.0%, the medically allowable CV is assumed to be 4.0%, the CLIA total error (TE) criterion is 10.0%. Current laboratory practices for setting control limits reveal a variety of approaches, such as statistical limits $\pm$ 2 or $\pm$ 3 times the observed method SD, clinical limits $\pm$ 2 or $\pm$ 3 times the medically allowable SD, or a fixed limit such as $\pm$ CLIA TE criterion. For a control material having a mean of 100, these various approaches would allow control limits to be set as the mean $\pm$ 4 mg/dL, $\pm$ 6 mg/dL, $\pm$ 8 mg/dL, $\pm$ 10 mg/dL, or $\pm$ 12 mg/dL, which correspond to statistical control rules of 1_{2s}, 1_{3s}, 1_{4s}, 1_{5s}, and 1_{6s}. Figure 3 shows a critical-error graph that describes the capabilities of different control rules and Ns for detecting the critical systematic error that would cause a laboratory to exceed the CLIA PT criterion. The critical systematic error here is 3.35 times the SD of the method [(10/2)-1.65].[5,6] The intersections of the critical systematic error line with the power curves for these rules with Ns of 2 show that error detection will vary from 0.99 or 99% to 0.01 or only 1%, depending on the control rule selected. Using a $1_{2.5s}$ control rule with N of 2 would give approximately 90% error detection with only 3% false rejections, which would provide a simple, cost-effective QC procedure for this application.

Insufficient technical quality management skills

Analytical quality management can be greatly improved by using simple error budgets, as represented by an analytical quality-planning model[5] that show the relationship between analytical total error requirements and performance characteristics of the measurement procedure (imprecision, inaccuracy) and control procedure (error detection, false rejection). Clinical requirements in the form of medically important changes, or decision intervals, can also be related to these same performance characteristics when pre-analytical factors are accounted for (such as within-subject biological variation) in the clinical quality planning model.[6] These models expand the total error budget to consider pre-analytical factors and QC performance, thus building in the margin of safety necessary to detect

Figure 3. Critical-error graph for glucose example

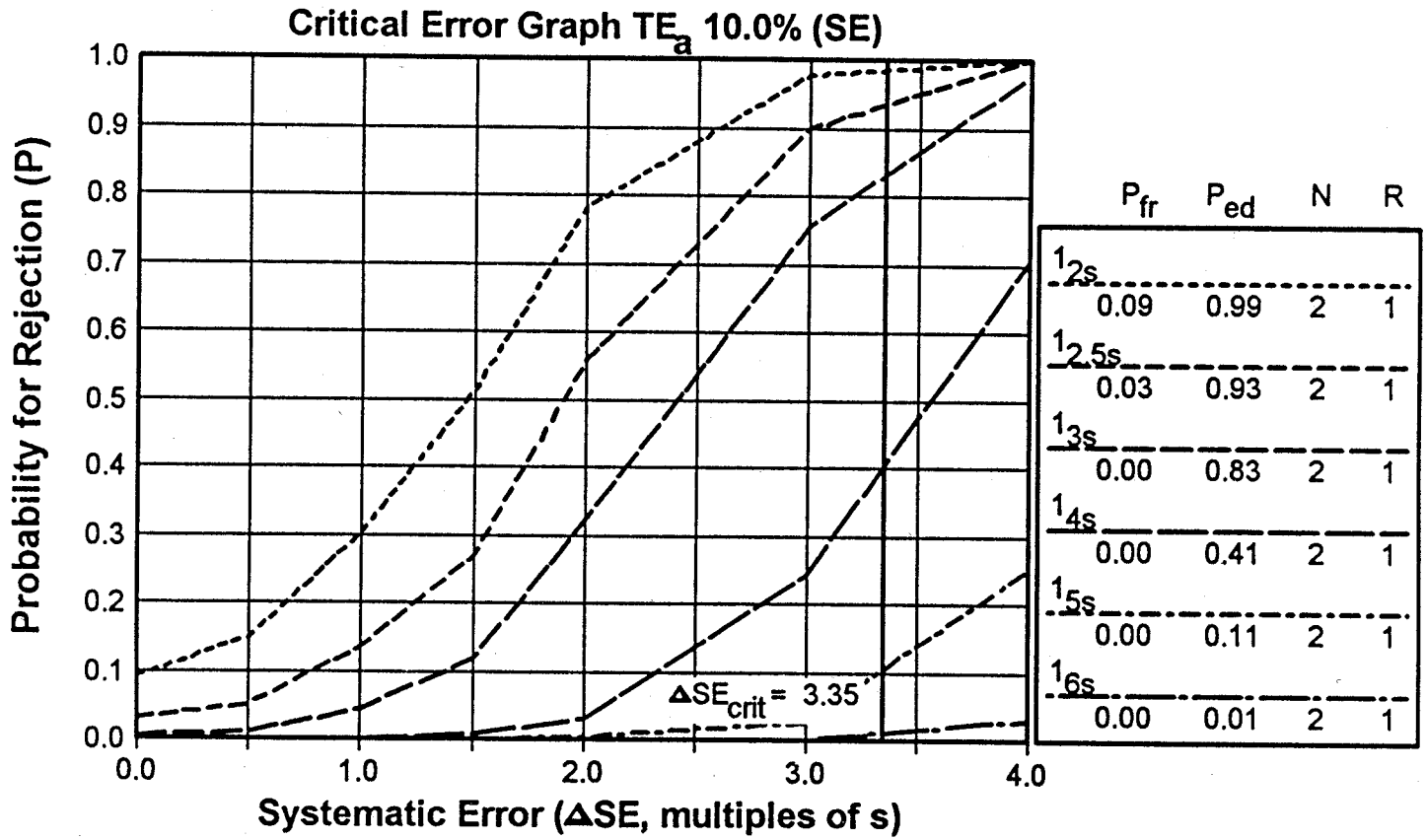

Figure 3

medically important errors.

Charts of operating specifications (OPSpecs charts)[11,12] display the relationship between allowable imprecision, allowable inaccuracy, and the necessary QC (control rules, N), as shown in Figure 4 for the glucose example discussed earlier. The different lines on the OPSpecs chart show the allowable inaccuracy and imprecision for different control rules and Ns, as shown in the key area at the right. The operating point represents the method's observed performance, in this case an imprecision of 2.0% and an inaccuracy of 0.0%. Lines above the operating point identify control rules and Ns that provide at least 90% detection of critical systematic errors. Of these candidate QC procedures, a $1_{2.5s}$ rule with N of 2 may be recommended for implementation based on its simplicity, high error detection, and low false rejection.

Managers need to understand QC planning tools, such as power function graphs, critical-error graphs, OPSpecs chart, and to apply them in planning and managing laboratory testing processes. The principles of total quality management tell us that problems occur because processes are imperfect, that process improvement is necessary to eliminate these problems, and that management is responsible for implementing appropriate processes. In laboratories, this means managers must put the appropriate measurement and control procedures in place.

Reduced operator skills

In the past, laboratories have been staffed by highly skilled analysts who were trained in laboratory technology and medical applications. These analysts generally had the skills to recognize problems and the discipline to solve them. They were dependable; therefore, the test results were dependable.

Today laboratory testing may be performed in different settings by a variety of operators who have a wide range of analytical skill and experience. Laboratories now must place a priority on having dependable processes that prevent problems from occurring and detect problems when they occur. This places a greater responsibility on manufacturers to provide highly stable measurement systems with built-in analytical quality assurance, particularly in those settings where it is known that operators will have little laboratory skill and experience. This also increases responsibilities for managers, technical specialists, and consultants who support laboratory testing in point of care settings.

Delays in implementing laboratory regulations

The delay in government implementation of a QC clearance process and the corresponding postponement of laboratory accountability for QC has resulted in a period of neglect for analytical quality assurance. Laboratories are waiting for manufacturers to provide the necessary QC instructions and, in the absence of QC clearance, are assuming that the present QC labeling will be adequate. During this time, the increasing pressure on cost control has taken priority over quality control, leaving laboratories focused on satisfying regulatory requirements and accreditation guidelines. Doing what's right to manage analytical quality may not be adequately defined by manufacturers' present QC labeling, or may not be completely identified by the lists of regulatory or accreditation requirements.

In addition, the lack of a mechanism for

Figure 4. Operating specifications for glucose example

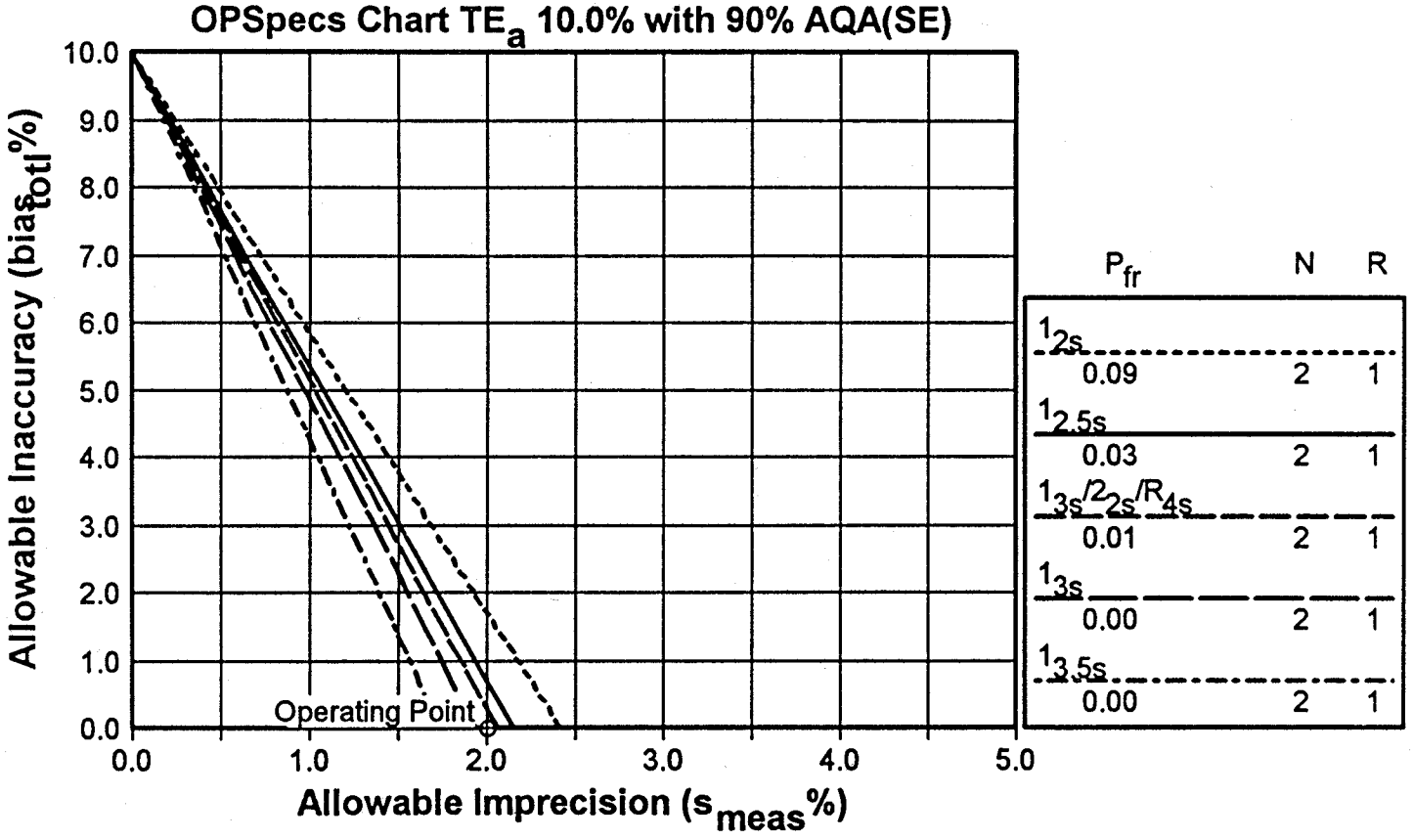

Figure 4

development and approval of new, non-traditional QC procedures may limit the potential applications of new technology. It may be more appropriate for manufacturers to make claims of defect rates for unit test devices and to provide data to substantiate low defect rates, in which case laboratories may find it necessary only to perform minimal checking when new shipments of materials arrive.

Summary

Although this discussion has focused on analytical QA, the issues identified should raise some concerns about the general *state of the practice* of laboratory QA. Are there reasons to think it's better for other quality characteristics? Are there firm data to show the relative frequency of problems and direct our attention to other areas? Are there audits of analytical quality that demonstrate a low frequency of problems in this area? Can we forget about analytical quality and move on to pre- and post-analytical problems? Can more quantitative patient management processes be built on top of our present foundation of analytical measurements? If not, how can laboratory testing be made more reliable?

I believe increased automation and computerization will be necessary to manage the quality of centralized and distributed laboratory testing processes. Analytical quality will have to be guaranteed through on-line or on-board quality control. The key inputs from laboratories or manufacturers will be the requirements for analytical quality and initial claims or initial estimates of method performance. Method performance data will then be collected, stored, and analyzed as part of an automatic QC process that selects and implements appropriate statistical QC procedures. Developing such an automatic QA process for analytical quality may also provide a model for other QA processes. Other critical quality characteristics will also require real-time monitors and control mechanisms to guarantee quality if process failures cannot be prevented.

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