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How to Construct and Interpret an Error Grid for Quantitative Diagnostic Assays; Approved Guideline

SAMPLE

This guideline describes what an error grid is, why it is useful, and how to construct one and interpret the information. Guidance is provided for manufacturers and for the clinical laboratory.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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How to Construct and Interpret an Error Grid for Quantitative Diagnostic Assays; Approved Guideline

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Abstract

Clinical and Laboratory Standards Institute document EP27-A—*How to Construct and Interpret an Error Grid for Quantitative Diagnostic Assays; Approved Guideline* describes what an error grid is, why it is useful, and how to construct it. An error grid illustrates the relationship between results obtained by one quantitative test to those obtained by a second one, while considering the diagnostic or therapeutic implications of the magnitude of the difference between the two results. Error grids inform users about the performance required to prevent potential patient harm. Once constructed, error grids can be populated with data from a measurement procedure comparison experiment. The proportion of data in each error grid zone is used to evaluate the clinical effectiveness of the measurement procedure

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Contents

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Foreword

Error grids are well known for performance evaluations of blood glucose monitors, but otherwise are little used. This guideline explains the usefulness of error grids to inform users about the clinical consequences of differences in results between a candidate and a comparative measurement procedure.

Guidance is provided on how to construct an error grid, how to locate the error grid zones based on the clinical errors that may be associated with differences in results between two quantitative laboratory measurement procedures, and how to estimate the proportions of differences in results that should be assigned to each zone. The concepts are illustrated with examples.

Key Words

Allowable total error, error grid, limits of erroneous results

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How to Construct and Interpret an Error Grid for Quantitative Diagnostic Assays; Approved Guideline

1 Scope

This document explains how to construct and use error grids to evaluate the clinical acceptability of quantitative diagnostic measurement procedures based on the potential harm that may be caused by erroneous results.

This document is intended for use by developers of measurement procedures—including laboratory-developed tests—and by clinical laboratories.

2 Introduction

An error grid is a simple nonparametric graphical tool for interpreting data from an experiment comparing a candidate measurement procedure to a comparative measurement procedure when testing the same group of patient samples. An error grid interprets the data in terms of the severity of potential harm to a patient from diagnostic or therapeutic errors that may be caused by differences between the results obtained by the two measurement procedures.

The error grid displays the data on an X-Y plot, where X = comparative measurement procedure and Y = candidate measurement procedure. The plot is further divided into zones that show how much error is problematic at different concentrations. It separates the magnitude of errors into a hierarchy—small errors may be tolerated with minimal risk to the patient, whereas large errors are likely to cause patient harm. Thus, there are limits that bound a region of allowable errors, called Zone A, where it is desirable to contain most of the data (see the light gray area in Figure 1); limits that bound another region of unacceptably large errors, called Zone C, where there should be no data (see the dark gray area in Figure 1); and the intermediate region representing moderate errors, called Zone B (see the white area in Figure 1), where it is acceptable to have a small percentage of the data. The error grid evaluates the candidate measurement procedure in terms of both the percentage of results within the desirable range and the percentage of unacceptably large errors.

An error grid analysis is most appropriate for interpreting the agreement of results from two measurement procedures using many patient samples, eg, approximately 100 or more. When there are relatively fewer patient samples, eg, approximately 40 or less, there is less confidence in the interpretation of the data and error grids may not be appropriate.

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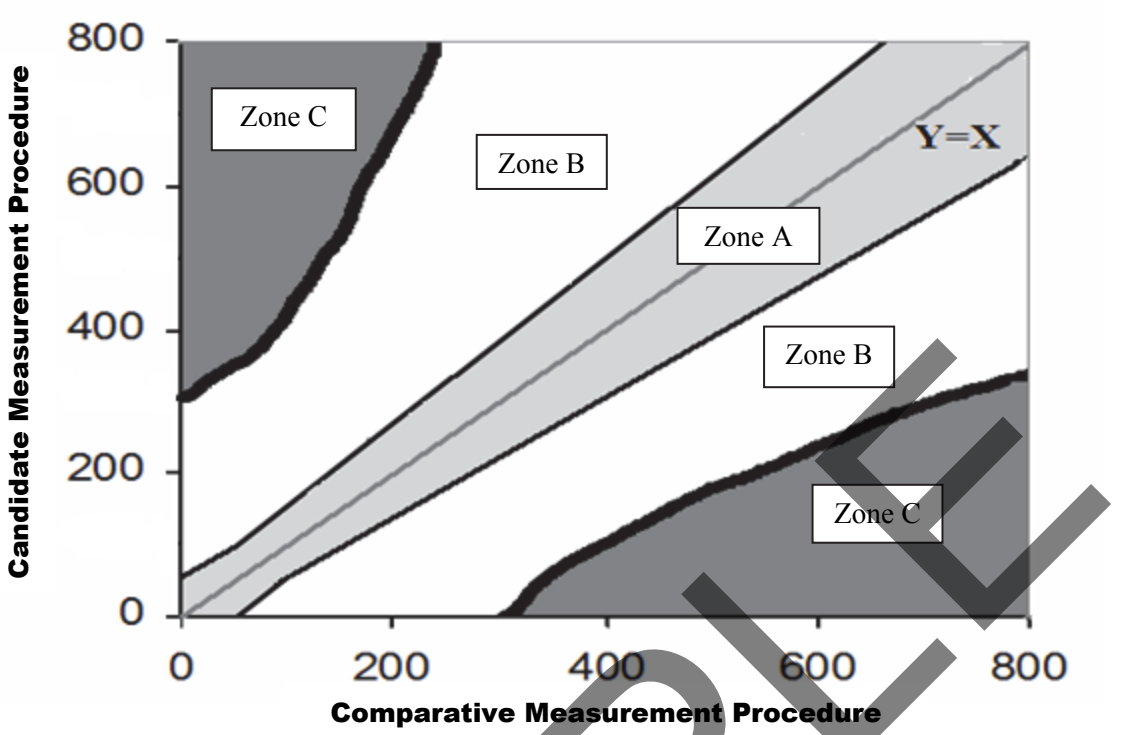

Figure 1. A Generic Error Grid

2.1 Error Grids History

2.1.1 The Clarke Error Grid

The Clarke error grid (see Figure 2) was designed for evaluating the performance of self-monitoring of blood glucose (SMBG) systems used by diabetic patients.[1]

The zones were determined based on the following clinical practice guidelines: (a) the "target" glucose interval was 70–180 mg/dL (3.9–10.0 mmol/L), with corrective treatment required only if a glucose reading was outside that interval; (b) any treatment that caused the glucose concentration to go outside that interval was inappropriate; and (c) failure to administer corrective treatment when the glucose concentration was less than 70 mg/dL (3.9 mmol/L) or greater than 240 mg/dL (13.3 mmol/L) was inappropriate. The zones were labeled from A to E, corresponding to different levels of risk of harm caused by differences in measured concentrations. Zone A was the region where the SMBG measurement and the comparative measurement were close enough to be considered clinically equivalent, ie, they would both lead to the same treatment decision. Zone B was the region where the erroneous SMBG measurement would lead to benign or no differences in treatment. Zone C was the region where the erroneous SMBG measurement could result in either excessive or unnecessary treatment based on falsely increased or decreased SMBG measurement when the actual blood glucose was within the target range. Zone D was the region where the SMBG measurement was erroneously within the target range, when the actual blood glucose was above or below the target range, potentially resulting in a failure to treat. Zone E was the region where the erroneous SMBG measurement could lead to treatment opposite to that which is indicated by the true blood glucose, ie, the SMBG measurement was falsely low when the actual blood glucose was high, or vice versa.

The zones in the Clarke error grid are irregularly shaped, and furthermore it is possible to move from Zone A to Zone D or from Zone B to Zone E without passing through the intermediate zones. For example, when the true glucose concentration is 58 mg/dL (3.2 mmol/L), an SMBG meter reading of 70 mg/dL (3.9

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The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management 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. The quality management system approach applies a core set of "quality system essentials" (QSEs), basic to any organization, to all operations in any health care service's path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

EP27-A addresses the QSE indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
		M29				X C54 EP05 EP09 EP21					

Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver the laboratory's services, namely quality laboratory information.

EP27-A addresses the clinical laboratory path of workflow processes indicated by an "X." For a description of the other document listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
C54		C54			X C54	X		

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Related CLSI Reference Materials*

C54-A-IR **Verification of Comparability of Patient Results Within One Health Care System; Approved Guideline (Interim Revision) (2012).** This document provides guidance on how to verify comparability of quantitative laboratory results for individual patients within a health care system. A CLSI-IFCC joint project.

EP05-A2 **Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition (2004).** This document provides guidance for designing an experiment to evaluate the precision performance of quantitative measurement methods; recommendations on comparing the resulting precision estimates with manufacturers' precision performance claims and determining when such comparisons are valid; as well as manufacturers' guidelines for establishing claims.

EP09-A2-IR **Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Second Edition (Interim Revision) (2010).** This document addresses procedures for determining the bias between two clinical methods, and the design of a method comparison experiment using split patient samples and data analysis.

EP21-A **Estimation of Total Analytical Error for Clinical Laboratory Methods; Approved Guideline (2003).** This document provides manufacturers and end users with a means to estimate total analytical error for an assay. A data collection protocol and an analysis method that can be used to judge the clinical acceptability of new methods using patient specimens are included. These tools can also monitor an assay's total analytical error by using quality control samples.

M29-A3 **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Third Edition (2005).** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.

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